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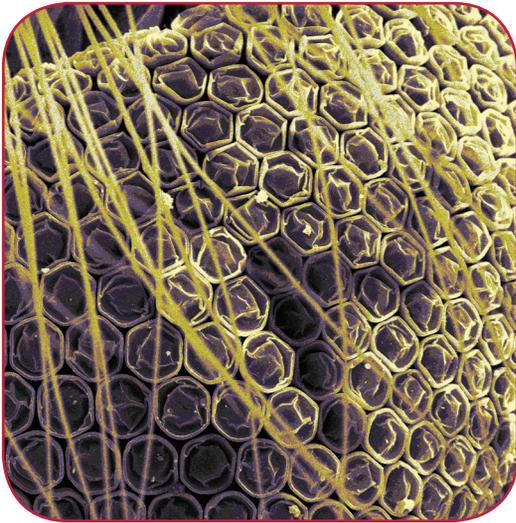
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COVID-19 and digital competencies among young physicians: are we (really) ready for the new era? A national survey of the Italian Young Medical Doctors Association

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Abstract

Background. Digital health (DH) is nowadays fundamental for physicians. Despite the improvement of information and communications technology (ICT), Italian medical doctors' (MDs) education system seems inadequate in this area. Moreover, due to the COVID-19 pandemic, societies are waking up to their limitations. The aim of this paper is to analyze the Italian *status quo* in DH.

Methods. The Italian Young Medical Doctors Association (Segretariato Italiano Giovani Medici - SIGM) proposed a web-based survey to assess DH awareness and previous knowledge among young doctors. Investigated areas were: big data, -omics technology and predictive models, artificial intelligence (AI), internet of things, telemedicine, social media, blockchain and clinical-data storage.

Results. A total of 362 participants answered to the survey. Only 13% had experience in big data during clinical or research activities, 13% in -omics technology and predictive models, 13% in AI, 6% had experience in internet of things, 22% experienced at least one telemedicine tool and 23% of the participants declared that during their clinical activities data collection was paper-driven.

Conclusions. Three categories of MDs, high-tech, low-tech and no-tech, can be identified from the survey-based investigation. Our survey's results indicate an urgent need for integration of pre- and post-graduation training in digital health to provide adequate medical education.

Key words

- medical education
- information technology
- artificial intelligence
- innovation
- digital health

INTRODUCTION

Contemporary healthcare has very tight relations with digital technology: from clinical data storage and data analysis to communication procedures, medical doctors (MDs) need to interact more with digital devices every

day. Digital health (DH) represents the bridge between digital technology, healthcare and society able to enhance healthcare delivery effectiveness [1] and make medicine more personalised and precise [2].

Being a wide and heterogeneous topic, DH started

with the gradual conversion of patients' data from physical to digital electronic records [3], until digital medical record (DMR) became the primary mode of nonverbal communication [4]. The accuracy and speed of digital computing gave the opportunity to store and systematically analyze a huge amount of clinical data, opening two innovative fields: big data analysis, empowered by distributed learning [5], and the -omics approach, ranging from genomics [6] to radiomics [7]. In this scenario, a monodisciplinary information and communications technology (ICT) approach is not enough: a cross-cutting figure with a medical background and DH skills is required to construct – for instance – large databases within a multicenter consortium or to validate high-tech DH tools [8-10]. Moreover, as it is the case of companies from other fields, healthcare institutions digitalisation must be guided by dedicated professionals such as a chief digital officer (CDO). However, considering the complexity of health workflow and the need for clinical pathways decision-making, the CDO should have a medical background [11].

Another topic of DH is artificial intelligence (AI) [12]. From pattern recognition [13] to process identification and enhancing [14], AI is remarkably interesting for every scientist or high-tech company. However, a major challenge of AI consists in the operators' frequent unawareness of the process that leads to the results: can we trust an algorithm to "decide" a treatment without a full understanding of it? AI is, therefore, a hot topic also for ethical reasons, as documented by the "Rome call for AI Ethics", a declaration subscribed by some of the world's biggest companies and the Pontifical Academy for Life, where a new term has been coined to identify the application of ethics within the algorithm: the "algor-ethics" [15].

Moreover, DH is not only composed of several high-tech tools for predictive models, but allows personalised clinical choices and empowerment of the clinical human intelligence. Several applications are developed every day for communication and tele-consultation and specific companies are created to provide online services for distant medical evaluation of the patients and e-health [2, 16].

Furthermore, in the face of the COVID-19 pandemic, societies are waking up to the limitations of their health care system [17]. In this context, DH role in providing tools, instruments and services could be noteworthy: from AI applications [18] to the opportunity of proposing video consultation instead of the traditional clinical examination in order to contain the infectious risk [19].

DH relevance is growing rapidly. Therefore, governments and companies should invest a consistent share of their resources in it and steer political choices in its favor [20]. In addition, much literature shows the impact of high-tech research in medicine [21]. Therefore, a digital-skilled profile is advisable for any professional involved in healthcare [22-27]. Despite its exponential growth in complexity, currently a specific training course in DH is not sufficiently provided in MD graduation programs yet [28-30].

To the best of our knowledge, there are no scientific experiences reporting the Italian situation in terms of

competences acquired in DH for junior MDs, who should become leading actors in the digitalisation of Italian healthcare. In order to promote an adequate DH education, a National project called VALIDATE Project (Value-bAsed Learning for Innovation, Digital health and Artificial inTelligenceE) has been launched. It has also been recognised by the Italian Ministry for Innovation and Digitalisation. As a first step for this project, the current condition of DH awareness needs to be assessed, especially for young MDs who represent the future of Italian National Health Service (NHS). Moreover, this project pursues the will of EU Commission and EU Universities stakeholders to promote digitalisation in medical education [31].

The aim of this paper is to analyse the Italian *status quo* regarding DH medical education to identify any critical issue and to propose adequate improvement strategies.

METHODS

Survey

The Digital Health Task Force of the Italian Young MDs Association (Segretariato Italiano Giovani Medici – SIGM), within the VALIDATE Project (Value-bAsed Learning for Innovation, Digital health and Artificial inTelligenceE), proposed a survey to recognise and describe the *status quo* of awareness and training in terms of DH and innovation technology.

From 12 to 19 February 2020, a cross-sectional, multicentre survey was conducted, thought, validated and anonymously self-administered through an online questionnaire to Italian young medical doctors.

The eligible people for the survey were: Italian medical students in the last two years of their studies, young medical doctors aged <35 years (including newly-graduated medical doctors), medical residents and specialized MDs (residency obtained within 3 years) in all medical fields as well as general practitioner (GP) trainees and GPs (diploma obtained within 3 years), practising in all Italian regions.

The survey was composed of 21 questions, organised into seven thematic areas where the first area explored the general characteristics of participants such as I) title, discipline and University. The next areas investigated awareness and knowledge about II) big data; III) -omics technology and predictive models; VI) artificial intelligence (AI); V) internet of things; VI) telemedicine, and finally VII) social media, blockchain and clinical-data storage.

For each section, 3 questions were explored: 1) knowledge about clinical applications of that specific technology into their medical area of interest; 2) experience of colleagues working in that field; 3) direct involvement in clinical or research activities into that field.

Development of the questionnaire was informed by a literature review whereas content validity was tested through online discussion and by collecting feedback from external experts. Previous to the launch of the survey, the questions were also pilot tested among 10 young doctors. The questionnaire was developed on SurveyMonkey (SurveyMonkey Inc., San Mateo, CA, USA) and was distributed via mailing list and social

media (Facebook, Whatsapp, website) of the SIGM network. Convenience sampling was chosen for the study, according to the nature of the study population and considering the impossibility of adopting different sampling strategies.

Statistical analysis

The results were reported with a descriptive analysis and further discussed within the Digital Health Task Force of SIGM in a dedicated web conference. The nature of the study (pilot), the potentially small sample size due to the recruitment method, as well as the objective of the study itself, which aims to offer a qualitative description of the results, led to not considering further statistical analysis from the accrued sample.

RESULTS

Within the study period (from 12 to 19 February 2020), the survey was proposed to 401 young medical doctors or medical students by mail. The number of users reached through social media is not strictly quantifiable, making it impossible to calculate the total response rate. A total of 362 Italian young medical doctors completed the survey.

More than half of them (57.2%, n. 206) were resident MDs, while 13.8% (n. 50) were MDs without any further post-graduated training course, 9.7% (n. 35) were medical students, 9.4% (n. 34) were specialist MDs, 6.9% (n. 25) were general practitioners (GP) in training, 1.7% (n. 6) were MD doctor of philosophy (PhD) students, and 1.4% (n. 5) were GPs (Table 1).

Participants were from all Italian regions, with 92.8% of Italian Medical Schools represented with at least one participant. Participants' medical background was het-

erogeneous: among the 52 different medical disciplines recognised in Italy, 79.2% were represented at least by one participant; intensive and critical care (14.2%), radiotherapy (6.9%) and Public Health (6.1%) were the most frequent ones.

Participants' answers to sections from II to VI are shown in Table 2.

Almost 39% (n. 141) of participants declared to have knowledge about clinical applications of big data into their medical area of interest, only 26% (n. 95) of participants had experience of colleagues working in the field of big data and 13% (n. 47) reported to be directly involved in the management of big data in daily clinical and research practice.

As for omics and predictive models, 30% (n. 107) of participants stated to have knowledge of these applications in their area of medical interest and the same trend of the previous domain was also shown in reporting both experiences of colleagues working in that field (27%, n. 99) and direct involvement in clinical or research activities (13%; n. 46).

About half of respondents (43%, n. 156) declared to have knowledge of AI appliance in their area of interest. The percentage of respondents decreases in reporting colleagues' experience (27%, n. 96) or direct involvement (13%, n. 46) in AI in daily clinical and research activities. The percentage of responders with knowledge, direct or indirect involvement in the field of internet of things were low, 20% (n. 71), 6% (n. 22) and 10% (n. 38) respectively. The questionnaire results showed that about half of the responders (53%, n. 191) have knowledge about telemedicine and its appliance to their discipline even if the rates of direct appliance (22%, n. 79) and indirect involvement (34%, n. 122) are lower than the median percentage.

Moreover, most of the participants seemed to deem relevant social media tools (82%, n. 294) in their work activities while a lower percentage was obtained regarding the relevance of blockchain tools (54%, n. 194).

In conclusion, junior doctors participating to the survey showed a heterogeneous practice in clinical-data storage tools use (Figure 1). Although the majority of participants declared to use electronic archives for clinical activities (76%, n. 274), only a few (8%, n. 28) reported to have the opportunity to share clinical data in a multicentre-based storage system.

DISCUSSION

This study represents a first attempt to investigate digital health knowledge in the heterogeneous world of Italian young MDs. The survey involved 362 young MDs in only 7 days, highlighting the strong interest and the relevance of the topic in this generation of professionals. However, results revealed a medium-low knowledge in the areas investigated with percentages ranging from 20% (knowledge regarding the applications of the internet of things) to 53% (knowledge of the application of telemedicine). A lower percentage was observed when the experience or the direct involvement of colleagues was investigated.

Results regarding the use of AI or blockchain are consistent with those emerging from a survey administered

Table 1
General description of survey participants

Survey responders		362
Region	Abruzzo	3
	Calabria	13
	Campania	33
	Emilia-Romagna	45
	Friuli-Venezia Giulia	1
	Lazio	114
	Liguria	1
	Lombardia	33
	Marche	1
	Piemonte	16
	Puglia	14
	Sardegna	6
	Sicilia	12
	Toscana	2
	Umbria	27
	Veneto	4
Not specified	37	
Status	Student	35
	Medical Doctor (MD)	50
	Resident MD	206
	General practitioner in training	25
	Consultant	34
	General practitioner	5
	MD and PhD	6
Not specified	1	

Table 2
Survey results. Dimensions and percentages

	Big Data	-Omics and predictive models	Artificial intelligence	"Internet of things"	Telemedicine
	Answered "Yes" (%)	Answered "Yes" (%)	Answered "Yes" (%)	Answered "Yes" (%)	Answered "Yes" (%)
Knowledge about clinical applications of that specific technology into their medical area of interest	141 (39)	107 (30)	156 (43)	71 (20)	191 (53)
Experience of colleagues involved in that field	95 (26)	99 (27)	96 (27)	38 (10)	122 (34)
Direct involvement in clinical or research activities into that field	47 (13)	46 (13)	46 (13)	22 (6)	79 (22)

in 2019 by the American Medical Association (AMA) in which doctors affirm to be familiar with these tools but only a few uses them [32]. Furthermore, we observed that young Italian doctors are more involved in the use of telemedicine tools and these results recall the ones published by AMA through its recent survey [32].

Moreover, in contrast with what would be expected according to the young target of this study, a homogeneous and clearly recognisable group was not identified. To exemplify, three different subcategories of MDs could be identified from what they answered to the survey. We could recognise: 1) high-tech junior MDs with relevant interest, knowledge and involvement in DH and innovation, that have seen and experienced new technologies in their clinical or research setting; 2) low-tech junior MDs, that seems to have had indirect involvement and not yet experienced the digital revolution in medicine; 3) no-tech junior MDs, who have just had a classic knowledge without any direct or indirect experience of DH.

Surprisingly, most of young MDs participating to the survey can be represented by the last two categories, demonstrating that giving a medical training to a digital native person does not necessarily mean to train a digital MD: to obtain a digital MD, a dedicated training with specific core competencies is needed.

According to the results of this survey, considering the

above categories, diversity in digital skills training must be considered and promoted [31]. To propose specific high-level education for selected MDs and to allow a complete generalized digitalisation of healthcare, two different training pathways would be recommended.

It would be beneficial to teach a dedicated core curriculum, with tight interconnection with other technical domain professionals (engineers, physicist, statistics, mathematics etc.). This future category of professionals has the responsibility: 1) to build a new semiology related to the tele-consultation, defining indications and contraindications of a telematic access to healthcare services rather than the traditional clinical evaluation; 2) to identify strong criteria for predictive models (-omics or AI based models) to be safely integrated in the routinely clinical practice; 3) to standardise the system of building clinical and research database storages; 4) to delimitate social network and new communication technologies within healthcare services. The task described above must not be left to the interest of the individual: a dedicated training is needed. On the other hand, in the third millennium a young MD unable to use technology is not more desired. With the rapid diffusion of new communication systems and with a general implementation of telemedicine, that is a global ongoing process, every MD should be trained to perform a tele-consultation (and therefore to know which semeiotic have to

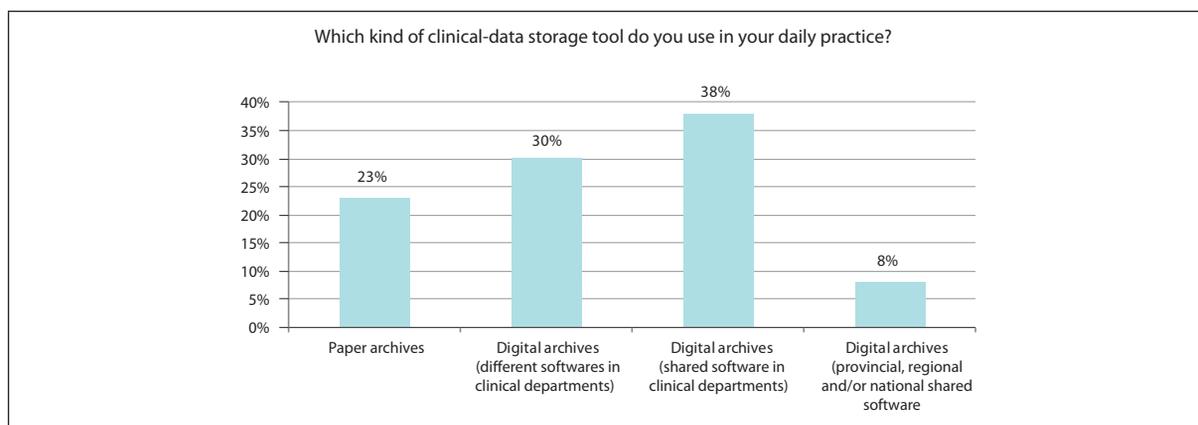


Figure 1
Answers on clinical-data storage tools.

be considered in that scenario); every MD should know which model (including -omics and AI models) is applicable to the different clinical settings and if it is reliable or not, which tool could be used or have to be recommended to give some information to the patients or to receive patient's communications, how to contribute with data acquired during their clinical activities to the main large database that will be available in next future.

To the best of our knowledge, only few papers analysed the *status quo* of junior MDs education in terms of DH education perspectives, but the few pieces of evidence in scientific literature highlight the lack of pre- and post-graduation specific training in DH [33, 34]. As reported by Jidkov *et al.*, in the United Kingdom (UK) health informatics training needs to be soon integrated [28], but a larger international evaluation needs the systematic assessment of the possibility to include DH skills for each medical education model. A professional with these skills needs to be also recognised in order to allow adequate healthcare workforce planning and to promote the role of chief digital officers within healthcare organizations [35]. Moreover, COVID-19 is turning out as a tremendous opportunity to accelerate this transformation both at cultural and at organizational level: we are learning the lesson of unpreparedness and we need to reinvent our way to provide healthcare.

According to the evidence added by this paper, it is urgent for the Italian NHS and for the Italian medical education system to define two different *core curricula*: the first one includes every skill or competence that MDs need for their clinical activities; the second one consists of a comprehensive *core curriculum*, for MDs that want to perform high-level research in DH or participate to the clinical definition of the semeiotic 2.0. The recent evolution of the Italian accreditation system of residential courses for MDs [36] is a useful framework to introduce, *inter alia*, the minimal requirement in terms of competences in DH.

The identification of MDs training as a critical control point is part of the strategic vision of the VALIDATE Project: the main bottleneck in health digitalization is not infrastructural, according to the fact that almost every physician owns a personal computer, but cultural and related to specific competencies.

Moreover, accordingly to the VALIDATE Project aims, a systematic definition of a comprehensive DH core curriculum for MD is required. The methodology of this educational training has to be related on one hand to the clinical setting of the trainee MD and,

on the other hand, to the complex institutional framework where the training experience is inlaid (e.g. pre-/post- graduation training, residency, general physician course, continuous medical education, others). For MDs with high-tech features, a second dedicated training program should be defined, preferably implemented in a PhD course or a specific master.

This study has many limitations. First, the sample size and the sampling methods do not ensure the representativeness of all the Italian young medical doctors category; moreover, the modality of recruitment does not allow to analyse the relationship between total respondents and involved users. Second, as with most surveys, there is a possibility that respondents gave socially desirable answers. To minimise this potential bias, we ensured complete respondent confidentiality. Finally, questions about personal experience are subject to recall bias. Despite these limitations, this survey represents a systematic attempt to underline specific needs in Italian medical education.

However, this survey should be considered as an initial mapping to investigate the phenomenon of digital health in Italy among young doctors. It would be suitable in the future to further investigate medical doctors' awareness and propensities to DH, extending this investigation to senior doctors as well since they currently represent the largest slice of the Italian Health workforce.

In conclusion, in the era of evidence-based medicine, allowing improvements in DH only as an individual and spontaneous attitude is no more sustainable: the present and future of digital health education needs a strategic plan that encompasses training starting during healthcare education [33] and continues with a life-long learning approach [31].

Conflict of interest statement

All the authors have no competing interests.

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Authors' contribution

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The cost of caring during recent epidemics: a rapid review of risk factors, psychological manifestations, and strategies for its treatment

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Abstract

Background. During epidemics, health care workers (HCWs) are particularly exposed to the risk of secondary trauma. If not effectively addressed, the consequences of such psychological distress can progress to more severe conditions.

Methods. A systematic search of several databases on the effect of SARS, MERS, and COVID-19 epidemics on the mental health of HCWs was performed according to both the Cochrane Handbook for Systematic Reviews of Interventions and the WHO Rapid Review Guide for Health Policy and Systems Research.

Results. The 77 reviewed studies highlighted that work organization and individual characteristics can add to mental health risk. Providing adequate training to prevent infection and prepare HCWs to handle the epidemic, strengthening team work to improve organization, and ensuring appropriate protective equipment is available can help prevent risk of psychiatric illness.

Conclusions. Monitoring and addressing through tailored interventions the mental health consequences of pandemics in HCWs is necessary.

Key words

- health care workers
- Coronavirus
- mental health
- epidemics
- prevalence

INTRODUCTION

On March 11, 2020, the WHO Director General declared that a “novel coronavirus (SARS-CoV-2) causing a severe acute respiratory syndrome called COVID-19 had reached pandemic diffusion from its initial outbreak in Wuhan, China, in December 2019 [1]”. Since the very first weeks of the pandemic it became apparent that health care workers (HCWs) were among the professional categories at the highest risk of acquiring the infection [2], reporting a disproportionately higher number of deaths than the general population, [3, 4] and these numbers are expected to dramatically increase [5].

In addition to the risk of acute illness, physical disability and death, HCWs are also particularly exposed

to stress and to situations of discomfort with limited possibilities of resolution, producing negative effects either on their wellbeing and mental health or on the quality of care provided to patients [6]. These phenomena can be described as compassion fatigue or compassion stress. A number of factors contribute to this profession-related psychological distress including: the real and perceived increased risk of infection; the voluntary or forced self-isolation from family members for fear of infecting them; the experience of stigmatization (HCWs seen as “plague spreaders”); the prolonged exposure to death and suffering (including the death of colleagues and family members); the experience of being often the only caregiver of dying patients due to isolation policies; feelings of helplessness in treating a

disease for which an effective cure has not been found [7], the need to make ethically challenging treatment choices due to limited resources available [8, 9], and at the same time concerns of being sued for malpractice by family members of deceased patients [10]. Moreover, during the COVID-19 pandemic, many doctors and nurses lacking specific training and experience have been diverted to wards managing infected patients, enduring an overwhelming workload, scarcity or absence of personal protection equipment (PPE), and overexposure to widespread of misinformation through social media platforms [11].

If untreated, psychological distress of HCWs can further progress to more severe psychiatric conditions including major depressive and post-traumatic stress disorder [6]. Prolonged absences from work, which can result from infection and obligatory quarantine, may also be a consequence of burn out [6], putting an increased strain on already overloaded HCWs. Ultimately, the health consequences of psychological distress experienced by HCWs during a pandemic, if not effectively addressed may put the entire health care system, already under-resourced, at risk of collapse [12].

The psychological consequences of epidemics on HCWs have been the object of several investigations over the course of the past several years: coronavirus epidemics, like those caused by SARS, MERS, and the ongoing COVID-19 pandemic, can be considered natural traumatic events that have been putting a great deal of burden on frontline workers, with both short and long term consequences for their mental health [13-20].

However, no systematic review, of which we are aware of, has been conducted so far on this topic.

Given the increased risk of psychological distress on frontline health care professionals involved at various degrees in the management of the COVID-19 pandemic, as well as during previous epidemics, the implementation of strategies to prevent, recognize, and treat mental health symptoms is needed [12, 21-23]. Hence, it is important to describe which actions have been already adopted during and after previous pandemic, and which one of these can be implemented now.

To this purpose, the present paper aims to review: 1) the HCWs psychological consequences of caring (risk factors for, psychological manifestations, prevalence of diagnosable mental disorders) during epidemics; and 2) strategies used for the prevention and treatment of these consequences.

METHODS

The methodology of the rapid review was guided by both the Cochrane Handbook for Systematic Reviews of Interventions [24] and the WHO Rapid Review Guide for Health Policy and Systems Research [25]. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was utilized to report the results of this review [26]. The protocol of the review have been submitted to OSF Registries on May 7, 2020 [27].

A librarian with experience in systematic review methodology (MCF) developed a search strategy in consultation with the authors. The searches were trans-

lated between databases for proper controlled vocabulary terms and syntax.

On April 11, 2020, systematic searches were done in the following databases: MEDLINE (Ovid), APA Psycinfo (Ovid), and Global Health (Ovid). The search was updated on May 4, 2020. To maximize sensitivity, the formal search used a combination of controlled vocabulary terms and free-text terms to capture the concept of psychological distress during an epidemic/ecological disaster by HCWs. An additional search of the grey literature was done to find articles in preprint servers (biorxiv.org/medrxiv.org), publisher's websites, and examining reference lists of included studies. No date limit was applied. The search strategy can be found in *Appendix*.

Eligibility criteria

Inclusion criteria for this review were: papers had to report outcomes in health care workers (HCWs) with reference to one of the aims of this review: risk factors for, symptoms of, prevention and treatment of mental health consequences of caring during an epidemic. Papers have to be published in peer-reviewed journals, and be written in English or Italian.

Study selection

Two reviewers (MF, FK) independently screened titles, abstracts, and full-text of relevant studies that met predefined inclusion criteria. Any conflict was resolved through consultation with a third reviewer or through discussion.

Data collection process

Using a standardized Microsoft Excel form, four reviewers (MF, FK, FV, ET) extracted the data independently. Another reviewer (FS) independently checked the data for consistency and clarity.

RESULTS

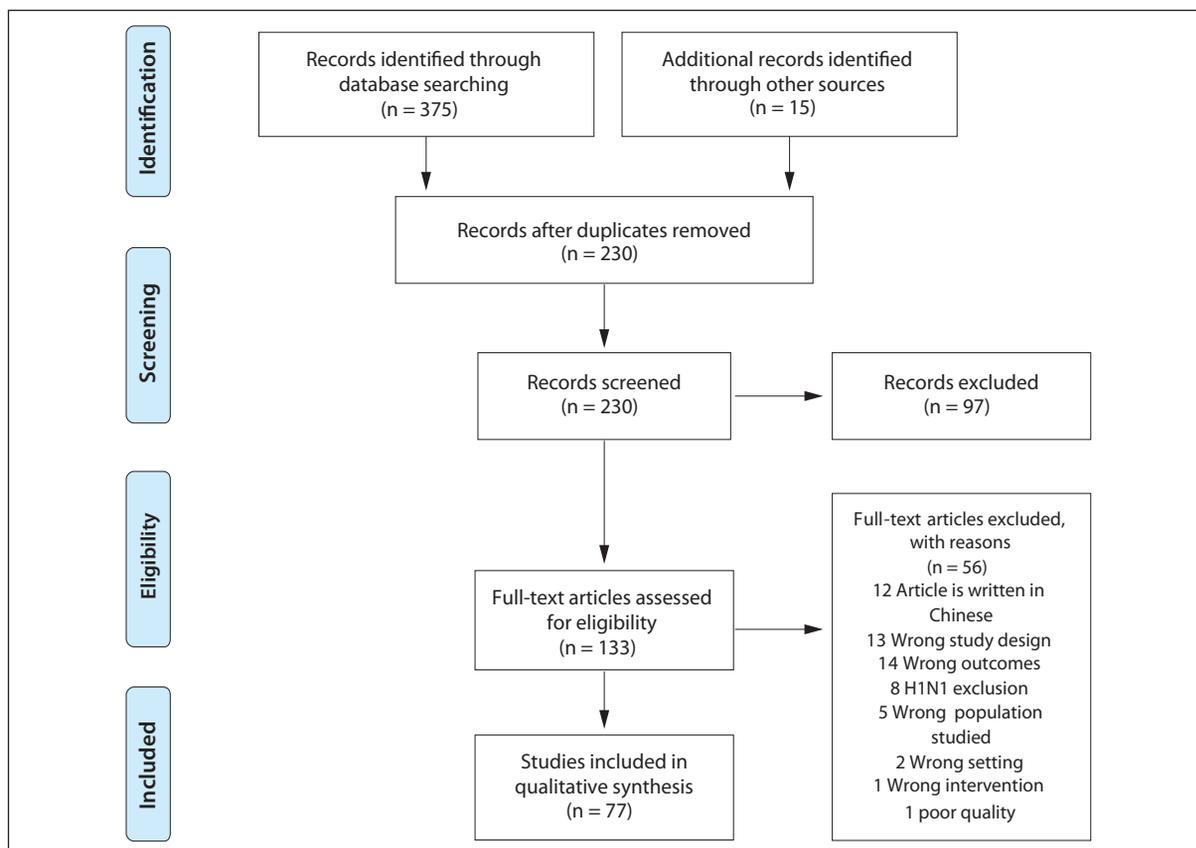
Characteristics of the included studies

The initial search yielded 375 studies, which were pooled in EndNote (endnote.com) and de-duplicated to 215. This set was uploaded to Covidence (covidence.org) for screening. An additional 15 articles were found outside of the database search.

There were 133 relevant studies for full text screening. Of those, 77 articles were selected for this review as they met eligibility criteria; only peer-reviewed articles were retained. Details of papers excluded at each screening stage is included in the *Figure 1*, and detailed in the *online Supplementary Material*.

Table 1 (available online as *Supplementary Material*) shows a summary of the 77 studies included in this review: 71 were original papers, 52 of which had a cross-sectional design, and six were reviews. Most papers focused on the SARS epidemic (n=49), while the remaining studies focused on MERS (n=5), and COVID-19 (n=23). All studies were published during the past 17 years, across eleven countries.

Despite the great variability in the methods and the format of the studies examined, all papers were included in the discussion, and limitations were acknowl-

**Figure 1**

PRISMA 2009 Flowchart of the screening process of the articles included in the review.

Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(7): e1000097. doi: 10.1371/journal.pmed1000097

edged. Here we summarize the findings according to the aims of this review: 1) the HCWs psychological consequences of caring (risk factors for, psychological manifestations, prevalence of diagnosable mental disorders) during epidemics; and 2) strategies used for the prevention and treatment of these consequences.

Risk factors for psychological symptoms

In total, 46 papers identified risk factors for psychological distress during epidemics (*Table 1a, Supplementary Material*).

HCWs suffer higher levels of distress compared to non-HCWs [28]. HCWs working during a pandemic carry the burden of fears of contagion and of infecting others [29], feelings of frustration due to the uncertainty in walking an uncharted (medical) territory, and feeling lonely as a result of forced physical isolation [28].

Compared to the non-clinical personnel, HCWs that worked in high risk departments treating respiratory infectious diseases were twice more likely to suffer from depression and anxiety [28]. Chen *et al.* pointed out that resuscitation maneuvers that can put HCWs at higher risk of contracting infection were associated with greater distress [30] among nurses during the peak of the SARS outbreak. Shifts with longer working hours [29, 31, 32], being a frontline worker [33, 34], and contact with SARS patients were correlated with ei-

ther more anxiety, depression, and post traumatic stress disorder (PTSD) [34, 35], somatic anxiety [36], with emotional exhaustion [37, 38], state anger [38], and the onset of new psychological symptoms [39]. Many reported that, within health care roles, being a nurse put the subject at higher risk of developing psychological symptoms, compared to other health care professionals [13, 18, 40-45]. However, having an intermediate technical title seems to carry a risk for psychological distress as well [31]. General practitioners involved in the care of SARS patients also showed higher psychiatric comorbidity than traditional Chinese medicine doctors; this higher prevalence was correlated with post event trauma and stigma [46].

The lack of preparedness of the team to face the epidemic, both in terms of skills as well as provision of adequate PPE, was a common risk factor. Chen *et al.* highlighted that, for emergency department staff, changes in care pathways, working in high risk units, and inadequate PPE were risk factors for higher levels of stress during SARS outbreak [47]. Isolation, high work intensity and pressure, witnessing mortality, wearing protective clothing every day, and handling hazardous materials triggered anxiety and sleep disturbances [48]. The shortage of PPE was one of the factors mostly correlated with feelings of worrisome, pressure, frustration [28], and burnout [49].

HCWs reported stress mostly being related to feelings of uncertainty, inadequate staffing and PPE, and fears of nosocomial spread [42]. Moreover, tension between team members interfered with team work [42]. Working in adverse workplace environments, holding numerous responsibilities, lacking proper support and feedback from supervisors were associated with lower adherence with infection control measures by HCWs [50]. Part-time employment status was associated with loss of sleep, loss of self-confidence, inability to make decisions [44].

Training and years of health care experience were inversely associated with developing a new psychiatric disorder [51]. Younger age was, in fact, associated with higher prevalence of anxiety, depression, PTSD, and sleep disturbances [2, 52]; it was also a risk factor for stress symptoms [45]. Younger age was also associated with post traumatic morbidity [53].

Being forced into quarantine was recognized as a risk factor for more severe psychological outcomes, such as depressive symptoms [54, 55], PTSD [2, 21, 54, 56, 57], insomnia [18, 58], emotional exhaustion [18, 58], anger [17, 37, 38], avoidance behavior [37], sleep disturbances [17], anxiety [55]. Social isolation, typical of quarantine measures, has been identified as a risk factor for anxiety [13] and sleep disturbances [48].

Being infected was associated with depressed mood, fear of social contact, and fatigue in 20% of patients (of whom 30% were HCWs) [59].

Social factors also contributed to poor psychological adjustment: specifically, being a woman [31, 60, 61], having children [13], being the only child who can support parents in need [62]. Marital status has been reported to play a role as well: a study reported that being single as compared to be married increased the risk for experiencing psychiatric symptoms [63], however it has also been reported that being married compared to be not married was associated to worst psychological adjustment [41, 53]. Living in rural areas was a risk factor for insomnia, symptoms of anxiety, obsessive compulsive disorder, and depression [64].

Premorbid psychological traits, such as neuroticism, and attachment features were identified as contributors to a higher severity of somatic symptoms [28, 65]. Pre-outbreak traumatic experiences were predictive of post-outbreak level of depressive symptoms. In Toronto, stress mostly manifested in HCWs in the forms of maladaptive coping behaviors, such as self-blame, hostile confrontation, and avoidance [20]. Past history of a mental health disorder was a risk factor for developing a new psychiatric illness [51]. More specifically, a past history of mood disorder [52], and current depressive affect were risk factors for PTSD [34].

Post traumatic morbidity was associated with less humor, less venting, and less acceptance [53]. Finally, having a physical illness contributed to increase the risk for developing different psychiatric symptoms [21].

Prevalence of psychiatric symptoms and diagnoses

Twenty-three studies in total reported the results of administering structured diagnostic instruments for various psychiatric disorders in the HCW population

(Table 1b, Supplementary Material). During the SARS outbreak, Sim *et al.*, reported that, out of 277 respondents (91 doctors and 186 nurses), 20.6% of physicians in primary care settings displayed psychiatric morbidity [53], a proportion similar to that observed by Tham *et al.* in the emergency departments (18.8%) [66]. The incidence of any psychiatric disorder can be as high as 5% among HCWs, even up to two years after an epidemic, as outlined by Lancee *et al.* [51]. Kang *et al.* [67], interestingly, grouped the results of a survey administered to 998 HCW in four progressive level of severity of mental health disturbances (which included rated scores for anxiety, depression, impact of stressful life events, insomnia): 36% had subthreshold symptoms, 34% mild, 22.4% moderate, and 6.2% severe.

Trauma-related diagnoses

The majority of the studies focused on trauma-related diagnoses. Acute stress trauma was present in 5% of HCWs during SARS outbreak, and it was mostly related to the quarantine [58]. During the peak of the SARS epidemic, 11% of nurses, more frequently those who worked in high-risk units, surveyed in Taiwan had a stress reaction syndrome which can include anxiety, depression, and somatization [30], lower than the 17.7% of the 124 emergency department HCWs in Singapore who had post-event stress (more frequent in nurses vs physicians) [66].

PTSD diagnosis was investigated in 13 studies. Sim *et al.* reported that 9.4% of HCWs within a primary health care setting (doctors and nurses) had post traumatic morbidity [53]. The score for likelihood of PTSD was higher in clinical staff compared to non-clinical staff, in a study conducted by Son *et al.* during MERS [35]. PTSD diagnosis was present in 33% of HCWs in the SARS units [52]. According to Jung *et al.*, the majority of the nurses experienced PTSD, half of them with the full level of symptoms [68]. The SARS outbreak was traumatic for the vast majority of medical staff, according to Lin *et al.* [32], with emergency department HCWs suffering more severe symptoms of PTSD when compared to the staff from the psychiatric ward [32]. 7.7% among 470 HCWs surveyed (76.8% were either physicians, nurses, or allied health care professionals) expressed clinical concern of PTSD [22], with higher trauma scores observed in non-medical health care workers in Singapore [22].

During the SARS outbreak, HCWs in high-risk wards showed elevated levels of stress similar to those suffered by HCW from low-risk units. However, one year later, high-risk HCWs not only had higher stress levels compared to those at low-risk, but their distress was associated with higher rates of anxiety, depression, and PTSD symptoms [33].

Four studies showed that HCWs have a high risk to suffer from chronic levels of PTSD: in Canada, the incidence of PTSD was still 2% up to two years after the SARS epidemic [51]. One year after the SARS outbreak, HCWs at high risk reported chronic stress [33]. In the three years following SARS outbreak, high levels of PTSD symptoms were reported by about 10% among 549 HCWs [2]; three years later, high levels of

PTSD symptoms persisted in 22 of them (about 40%), especially in those with low household income or those being single [2]. Two months post SARS outbreak, approximately 20% among 661 participants (113 doctors, 548 nurses) presented PTSD symptoms [63].

Psychosomatic and sleep disorders

Psychosomatic disorders appeared to be common in HCWs during epidemics. Cao *et al.* reported 6/37 doctors and 11/19 nurses complained of mild body discomfort in the absence of COVID-19 infection in fever clinics [69]. Somatization was more prevalent in HCWs compared to non-HCWs, according to Zhang [64]. High-risk HCWs reported a large number of physical and psychological complaints; moreover they expressed worries about fears of contagion during social contact, despite having confidence in measures to control the spread of the infection [33]. Less-specific signs of stress were reported by Tam *et al.* [45], and Phua *et al.* [70].

Insomnia was present in 38.4% of 927 medical HCWs during the COVID-19 outbreak [64], and it was higher in SARS nurses than in non-SARS nurses (37% vs 9.7%) [52].

Depressive symptoms

Depression had higher prevalence in nurses working with SARS patients vs nurses caring for non-SARS (38.5% vs 6.7%, respectively) [52]. During the COVID outbreak, Tan *et al.* found that 8.9% of 470 HCWs screened positive for depression [22]. Rates and severity of depression vary according to profession and risk: depression was more frequent in medical HCWs vs non-medical (12.2% vs 9.5%) [64]. During the COVID epidemic in Fujian provincial Hospital, Lu *et al.* found that mild to moderate depression was present in 11.8% of medical staff, and severe depression in 0.3%: the severity of depression was more pronounced than in non-clinical staff, particularly in HCWs from high risk units [71]. One to two years after the the SARS epidemic in Canada, the incidence of new episodes of major depression among active HCWs was still 4% [51].

Anxiety and obsessive compulsive symptoms

Symptoms of anxiety frequently feature among the psychological consequences of epidemics on HCWs. Anxiety was reported as being higher in medical HCWs compared to non-medical HCWs (13.5 % vs 8.5%) by Zhang *et al.* [64]. However, Tan *et al.* found that the prevalence of anxiety was higher among non-medical HCWs than medical personnel [22]. Lu *et al.* [28] found higher levels of anxiety in medical staff, compared to administrative staff; within medical staff, 22.6% reported mild to moderate and 2.9% severe anxiety. According to Poon, staff who had exposed to SARS patients suffered higher level of anxiety as compared to those who had not been exposed [29]. Anxiety scores correlated with the discomfort from the use of PPE [29], and with burnout scores regardless of contact with SARS patients or role as front-line worker.

Only one study reported obsessive compulsive disorder symptoms which were present in 5.3% of medical HCW surveyed vs 2.2% of non-medical HCW [64],

however the assessment of premorbid condition was not performed.

Lastly, but not for importance, the prevalence of burnout was reported higher for nurses working in the emergency department during MERS outbreak, than in those assigned to other departments [49].

Prevention strategies

Thirtyseven papers addressed this topic, but only seven studies reported on tested interventions aimed at preventing psychological distress in HCWs during or after an epidemic (*Table 1c, Supplementary Material*) [7, 19, 35, 38, 48, 72, 73].

Aiello described a resilience training developed after SARS. This intervention, directed at 1250 staff members, increased the confidence of participants in facing higher than usual demands; moreover, the feedback collected were used to tailor the actions implemented during the H1N1 outbreak. For example, the presence of senior staff was increased in order to oversee younger hospital members and to provide a stronger leadership. Immunization to HCWs family members was provided. Additional psychosocial support was offered. E-learning was also encouraged [72].

During the SARS outbreak in Taiwan, 116 nurses underwent an anxiety prevention program which include training, re-allocation of manpower resources, and the allocation of a mental health team. This program led to a reduction of anxiety after two weeks since its implementation, with a return to normal levels (pre-SARS) one month after the hospital returned to normal operations. Sleep quality also improved [73].

Maunder *et al.* reviewed approaches aimed at reducing HCWs distress by building resilience prior to the pandemic. The goal was to empower HCWs, especially nurses, by implementing organizational changes to reduce the caseload, and increase professionals' agency and autonomy [19]. Fiksenbaum *et al.* reported that levels of organizational support significantly reduced perceived SARS threat, emotional fatigue, and state anger in a sample of 333 nurses [38].

After the MERS outbreak, in South Korea a preventive program was addressed to 280 HCWs. It included strategies such as resilience-building programs, and debriefing sessions. HCWs benefit the most from interventions aimed at lowering perceived risk [35]. As already reported by Kim *et al.* during the MERS outbreak [49], Xiao *et al.* reported preventive social support measures implemented during the COVID-19 pandemic: these were helpful in reducing anxiety and stress levels, increased their self-efficacy but did not improve their sleep quality [48].

Finally, Ripp *et al.* describe the characteristics of an "Employee, Faculty, and Trainee Crisis Support Task Force" created in the Mount Sinai Health System early during the COVID-19 outbreak in New York City. This multidisciplinary team, composed of leaders from human resources, behavioral health and well-being from across the health system, employed a rapid needs assessment model in order to capture HCWs' worries and necessities. They focused the intervention in meeting basic needs (e.g. transportation, food, personal safe-

ty, childcare), communication (town halls, website, email), and psychosocial support (mindfulness, support groups, individual mental health services voluntary and offsite, 24/7 mental health crisis support, and mental health professionals deployed to units either virtually or in person) [7].

During COVID-19, Kang *et al.* [67] reported 36.3% of the HCWs in Wuhan had received psychological support materials, half of HCWs had accessed the psychological resources available online, but less than one in five had attended group counselling. Moreover, those who had the most severe presentation were also those who were less likely to request counselling directly from professionals.

As Shanafelt *et al.* pointed out [74], listening to the needs of HCWs directly can offer valuable guidance on how to tailor interventions and identify sources of anxiety. These keyworkers during listening sessions delineated leaders' roles during time of crisis: the leader should be able to understand the sources of concerns, recognize the manifestation of such worries, involve HCWs in the conversation about strategies to adopt, encourage HCWs to ask for help, legitimize the willingness to re-prioritize activities, and recognize HCWs efforts by expressing gratitude.

Interventions

Twelve papers, half of which were qualitative, provided insights regarding strategies to address the psychological consequences suffered by HCWs during an epidemic (Table 1d, Supplementary Material).

Maunder *et al.* identified that individual as well as systemic aspects mediate long-term adverse effects of epidemics. At the individual level, interventions, such as moral support and protection, mentorship or "buddying" programs, which reduce maladaptive coping, may decrease prolonged suffering. At the system level, provision of enhanced support training might reduce burnout and post-traumatic stress [20].

After the SARS epidemic, a qualitative analysis was conducted by Amaratunga *et al.* to describe key features and remaining gaps in hospital influenza emergency plans [75]. Employees had access to grief counseling (individual or group sessions), spiritual and psychological services, and counseling for PTSD. Web and telephone counseling were available for both affected individuals and their families. Workshops were specifically designed to assist workers and the workplace to resume optimal productivity. Actions included: 1) providing rest periods and relief to staff in all key positions, including management; 2) informing employees about their rights and obligations surrounding work refusal; and 3) instructions on how to apply for requests for redeployment. The qualitative analyses highlighted that the HCWs identified different areas that still needed tailored efforts: psychological support services, management responsibilities outline, immunizations planning, strategies to handle media, and professional development [75].

Three studies [16-18] focused on how to identify and manage psychosocial impacts of the SARS epidemic on HCWs. These studies proposed four distinct levels of strategies that included: i) training to HCWs to

gain confidence to perform under difficult conditions by engaging them in the overall planning [16, 18]; ii) managers as enablers of supportive relationships between HCWs [16, 18], and providers of up-to-date communications [17, 18], preparing employees on the consequence of the epidemic [17, 18], promoting psychological wellbeing [16, 18], providing educational intervention to manage fear [17, 18], and web base support for feeling less isolated [17, 18]; iii) addressing the immediate and longer term psychological needs of trauma-survivors [16]; iv) providing psychoeducation and signposting for insomnia anxiety and stress to every nursing unit involved in quarantine [17].

Seven articles reported actions taken early in the course of COVID-19 outbreak, such as 1) building a psychological intervention medical team to provide the medical team online courses on how to deal with patients' psychological difficulties [76]; 2) providing a psychological assistance hotline team, for supervision and problem solving advice, and group stress-release activities; 3) availability of a place where the staff could rest, and provision of food, and daily living supplies; 4) reinforce hospital security to manage non-compliant patients; 5) education activities to teach how to use PPE.

Huang *et al.* described all the activities put in place in Chinese hospitals during the COVID-19 outbreak: telephone and online counseling for frontline medical staff, early psychological support through strategies to reduce psychological stress, online consultation with psychiatrists; psychological training for the front-line medical staff (online, onsite, group); innovative psychological interventions through short videos, online games and self-help mental health handbooks; self-rated rating scales for medical staff with signposting according to results [77].

Jianget described advantages and limitations of a two-pronged (online and onsite) approach for psychological crisis intervention during COVID-19 in Shanghai [78]. Psychological care becomes an integral part of the comprehensive plan for the control of the epidemic: it is aimed to minimize the risk of infections among mental health providers and to reduce their exposure to trauma and stress. They identified four different degrees of at-risk populations in order to tailor treatment and set priorities: onsite services were offered to the two highest at risk populations (which includes front line staff regardless the severity of psychological distress), and 24/7 remote real time support to the others (which include the general public). Remote consultations minimized the risk of infection for health care professionals. However, they also reduced the ability to collect psychometric data and fully appreciate body language, integral parts of a full psychological and psychiatric assessment.

Kang provided a description of the multifaceted psychological interventions targeting medical workers in China during COVID-19 [79]. There were four psychological intervention teams in Wuhan: a) a front-door response team; b) a supervision team composed by senior psychologists; c) a specialist team (mainly psychiatrists) targeting health-care workers and patients; and d) volunteers covering a consultation hotline.

Ho *et al.*, in their commentary, outlined possible ar-

eas of intervention: such as online psychotherapy (CBT and Mindfulness-based therapy), psychoeducation for general population; peer support for HCWs [61].

Neto *et al.* further suggested the regional and national authorities should promote the establishment of mental health teams (with diversified professional profiles) dedicated to patients and HCWs [80]. The use of smartphones was encouraged to provide a clear communication channel and decrease isolation between HCWs and their family members. Clear communication with regular updates regarding the outbreak is useful to address HCWs sense of uncertainty. Safe psychological counseling service should be provided using electronic devices.

Greenberg *et al.* in their editorial outlined actionable items that healthcare managers need to design and implement to protect HCWs' mental health. These included the provision of training and safe forums to discuss the emotional toll of making morally challenging decisions. To deal with avoidance, staff should reach out to those who state they are too busy to have a conversation about their psychological difficulties. Trained peer supporters and a chaplain should be offered to professionals for mental health support. Single session debriefing approaches were discouraged in favor of meetings addressing moral injuries and what to look out in terms of psychological symptoms [12].

DISCUSSION

This rapid review covers three important areas of the psychological consequences of recent epidemics for HCWs, including the ongoing COVID-19 pandemic. It summarizes risk factors for HCWs psychological distress, common symptoms and diagnoses, and preventive strategies adopted in previous epidemics. It offers insights about possible actions that health care authorities and managers can adopt during or immediately after an epidemic.

Risk factors

Our review highlights that HCWs are at greater risk of developing psychiatric symptoms when compared to the general population. Both the type of work and its organizational factors, as well as personal factors can contribute to this risk. Nurses are especially affected, in particular those who work in high risk units in close contact with infected patients. A poorly organized structure where interpersonal relationships are inadequately managed and where practical support and protection, especially PPE, are lacking puts staff mental health at greater risk.

These findings need to be taken into account by health care managers and team leaders in targeting support and preventive initiatives. Care managers and team leaders should promote the planning, organization, and coordination of communication with and between professionals [81]. HCWs should receive clear, timely, and up-to-date communications on procedures and measures to be implemented in different contexts and their motivations. Workplace and time allocation should carefully organized by a clear assignment of roles and tasks, taking into consideration professional

skills and pre-existent health conditions. In addition, high level of cohesion and supportive climate between HCWs, moments of sharing between operative units, dissemination of the strategies and good practices, and recognition of the personal and professional contributions and efforts should be encouraged [81]. HCWs should also receive appropriate training to reduce the feeling of inadequacy, uncertainty, and lack of support by implementing distance trainings and technical reports. For example, training in communication with the patient's family members in the specific context of the pandemic emergency has become crucial.

Other risk factors include: having little work experience, a pre-existing chronic condition, having experienced trauma in the past, being a single woman, and having children.

HCWs should be provided of material support interventions such as provision of adequate PPE, the organization of places of recovery and rest in the context of work, support in the supply of necessities (e.g., food), the provision of dedicated housing to avoid return home or for the management of isolation, support in the management of children, and economic awards. Care managers and team leaders should promote HCWs' psychological well-being by disseminating individual support strategies (e.g., try to ensure a restful sleep, take a light and nutritious diet, practice physical activities, enjoy relaxing music, maintain contact with family even if remotely, avoid prolonged work overload, avoid overexposure to content and information through the media), and monitoring reactions related to discomfort (e.g., poor quality of sleep, poor or excessive appetite, fatigue, tension, and stress) [81, 82].

Prevalence of psychiatric diagnoses

Reviewed studies highlight a high prevalence of new psychiatric diagnoses in HCWs: as expected, PTSD, depression, anxiety and somatic disorders are the most common [83]. Two interesting findings are worth mentioning. First, during the outbreaks reviewed, the number of HCWs with PTSD symptoms can reach up to 57%. Second, the few studies with post-outbreak follow up show that this figure drops but remains still significant in the long term. These results both highlight the mental health price HCWs have to pay during the pandemic and underscore that symptoms, if left untreated, may become chronic. Long-term effects may affect HCWs performance, resulting in greater risks for patients and the system of care as a whole [84].

There is a need to better understand predictors of long-term mental health consequences among HCWs in pandemics. In the meanwhile, public oriented services, especially those whose mission is to provide care, should bear a trauma-informed focus in the organization of the daily clinical work. It can be useful to schedule meetings, also remotely, to allow HCWs to share their concerns and encourage support, with particular attention to those who have a history of mental health problems.

Preventive measures and interventions

Preventive interventions offered to HCWs before a pandemic outbreak need to address the following: pro-

viding adequate training to handle the epidemic and its specific professional demands, strengthening team work to improve organization and relationships, and ensuring appropriate PPE availability. During the pandemic, interventions should address several levels of needs: practical life needs (e.g. transportation, food, personal safety, childcare), communication needs (website, email), and treatment needs. These include psychosocial and mental health support such as mindfulness, support groups, individual mental health support, and offsite, 24/7 mental health crisis support, and mental health professionals deployed to affected units either virtually or in person. Key elements to support HCWs during an epidemic include organizational aspects of the work including the reduction of prolonged shift time and night shifts; ensuring adequate staffing by re-allocation and postponing of elective activities [85]; and enlisting retired personnel/military/government funded resources. Finally, team leaders should encourage and facilitate confidential screening for depression and suicidal ideation [86].

HCWs should be provided with psychological support interventions to prevent and treat stress-related conditions in the work environment and promote resilience. Psychiatric and psychopharmacological interventions should also be offered, when appropriate, within clinics dedicated to HCWs.

This review underscores the importance of mental health consequences of pandemics for HCWs, in the short and long term. The need for a centralized and coordinated control room [61] with mental health professionals and experts included in regional and national COVID-19 Task Forces to advise the government on mental health policies appears of paramount importance.

Strength of the review

A main strength of this rapid review is the ability to provide a timely update on a relevant global mental health issue, HCWs mental health during epidemics, combining available epidemiological data on previous and current strategies to address psychological consequences of the cost of caring for HCWs. Differently from previous similar studies, this review was registered on OSF, it adopted a comprehensive appraisal of available studies, a larger source of information (which included Global Health, preprint servers, publisher websites, and references of included studies) [87], with no date limit, guided by the contribution of an expert librarian.

Offering a full picture of risk factors, preventive measures, and intervention strategies, it suggests effective organizational and practical operational procedures and policies for countries that are in the early, mid, or late stages of a pandemic.

Limitation of the study

Many interventions, studies, and reviews of mental health impact on HCWs are certainly underway at the time of writing. Although broad criteria were used in searches, some papers might have been missed. However, the high number of studies included suggests that the search strategy was comprehensive.

CONCLUSION

Pandemics carry a significant risk to the mental health of HCWs. Timely, targeted and evidence-based actions are needed to avoid personal suffering and disability and to reduce services disruption, which has a cascade effect on society wellbeing as a whole.

This review underscores that psychological protection of HCWs is a key component of public health measures

APPENDIX

Ovid MEDLINE search strategy

Search line	Search string
1	mental disorders/ or anxiety disorders/ or obsessive-compulsive disorder/ or panic disorder/ or gambling/ or mood disorders/ or depressive disorder/ or affective disorders, psychotic/ or sleep wake disorders/ or somatoform disorders/ or hypochondriasis/ or neurasthenia/ or "trauma and stressor related disorders"/ or adjustment disorders/ or stress disorders, traumatic anxiety disorders/ or substance-related disorders/ or alcohol-related disorders/ or ("mental disease*" or "mental disorder*" or "mental health" or "mental illness*" or "mentally ill" or anxieties or anxiety or "obsessive compulsive" or panic or gambling or "eating disorder*" or mood disorder* or depress* or "affective disorder*" or psych* or "sleeping disorder*" or "sleep disorder*" or insomnia or "Somatic symptom disorder*" or "somatization disorder*" or "somatoform disorder*" or hypochondria* or neurasthenia or stress or traum* or adjustment disorder* or ptsd or "substance use").tw.
2	health personnel/ OR exp nurses/ OR exp physicians/ OR (clinician OR health care personnel OR healthcare personnel OR health care provider* OR healthcare provider* OR health care worker* OR healthcare worker* OR health personnel OR health provider* OR health care professional* OR healthcare professional* OR medical personnel OR medical professional* OR medical staff OR medical worker* OR medical workforce OR nurse* OR nursing assistant* OR paramedic* OR paramedical personnel OR physician*).tw
3	exp SARS Virus/ OR exp Middle East Respiratory Syndrome Coronavirus/ OR exp Influenza A Virus, H1N1 Subtype/ OR (H1N1 OR "Swine flu" OR "swine influenza" OR "Severe Acute Respiratory Syndrome" OR SARS OR "Middle East Respiratory Syndrome" OR MERS OR covid19 OR covid 19 OR nCoV OR CoV 2 OR CoV2 OR sarscov2 OR 2019nCoV OR novel coronavirus* OR new coronavirus OR 2019 novel CoV OR wuhan virus* OR "coronavirus 2019" or "2019 coronavirus" OR ((wuhan OR hubei OR huanan) and (coronavir* OR corona virus* OR betacoronavir* OR severe acute respiratory OR pneumonia*))).mp.
4	1 AND 2 AND 3

Note: The search was last updated on April 27, 2020.

to be addressed during an epidemic [31].

Given the recurrent nature of pandemics, involving more and more citizens due to globalization and easy mobility, more research is needed on how to better protect HCWs' mental health during the emerging scenario, to guide the implementation at national, regional, and local level of clear action plans, appropriately resourced and reviewed.

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Intangible benefits of clinical trials: a survey on a hospital research community

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Abstract

The ongoing pandemic is highlighting the strategic role of clinical trials as an essential step of biomedical research, with a potential life-saving impact on public health. Several studies have focused on the assessment of clinical trials' economic impact. Robust methods allow a reliable assessment of the impact of trials on population health in terms of new drugs development. This study shows the results of a survey administered to the research community of the IRCCS Ospedale Pediatrico Bambino Gesù. The goal of the survey was to assess how researchers' participation in clinical trials impacts on research capacity development, career improvement, health benefits, knowledge production. The study results suggest that clinical trials promote a significant improvement of research capacity by the development of scientific know-how, the creation of new research networks, the improvement of diagnosis and clinical decision-making skills, the openness to new therapeutic approaches, and the patient recruitment and data management capabilities. These results actually suggest that clinical trials lead to better care also because they contribute to create better physicians, and not only because they provide new drugs or devices. Economic benefits, patient recruitment and researchers' internal reputation have been highlighted as critical issues.

Key words

- clinical trials
- assessment
- impact
- survey

INTRODUCTION

There is a general global consensus on the importance of measuring the economic impact of biomedical research [1]. This has led to an extensive literature on the development and study of research impact models [2, 3]. However, there is no unique model for research impact analysis officially adopted in the EU [4]. Furthermore, an assessment model specifically dedicated to the impact of clinical trials on biomedical research centres conducting them, has not yet been developed [5, 6].

In Italy, universities and hospitals (but not yet regulatory authorities and policy makers) show a growing interest in the development of cost-benefit analysis models for clinical trials [7, 8]. However, there are no integrated models of analysis and evaluation that include the "intangible" benefits (i.e. not expressly economic or financial) of clinical research, i.e. how researchers' participation in a trial may impact on their professional and scientific growth [9, 10]. There are actually studies in the literature that have examined the impact of biomedical research on the research capacity of the scientific community. These studies are based on the so-called "Payback" [11, 12] impact assessment framework, which has been integrated with other variables to make it more robust and adaptable to different assessment scenarios [13]. One of these studies focuses

on the socio-cultural impact of biomedical research on the scientific community itself [14].

A recent Italian study, focusing on the factors capable of improving the attractiveness of a biomedical research centre, has analyzed how different professionals of healthcare companies involved in drug trials perceived the advantages and disadvantages of such trials [15]. Following this study (which also includes "intangible" variables), the main advantage of experimental activity is its capacity to attract new trials. The authors attribute this effect to the "signaling" value of scientific trials in terms of scientific excellence and quality of the investigators.

The study carries out a perception analysis on the responses of a sample of clinicians involved in clinical trials and belonging to the same research community. It has been carried within the IRCCS Ospedale Pediatrico Bambino Gesù (OPBG), specifically focusing on clinical trials, and it aims at measuring the benefits that clinical trial participation produces on a community of researchers in terms of research capacity development, scientific knowledge production, researchers reputation and career development.

The investigation was conducted in an Italian context, as there is still relatively limited evidence on the organization and management of clinical trials in Italy and there is the need of building awareness on the impact of

clinical research in a broader sense, not only economic, also considering the missed opportunities related to the lack of localization of the trials by companies.

METHOD

An *ad hoc* questionnaire was prepared to conduct the survey. Before starting the survey, the questionnaire was:

- presented informally to the OPBG principal investigators (PIs) to have their feedback and comments;
- tested with a group of volunteer young researchers to verify understandability, response times, effectiveness to research purposes.

The questionnaire is divided into two parts. The first part is on personal information and aims at segmenting responders on the basis of age and expertise. The second part explores the main benefits of trial participation for researchers and includes four blocks of variables:

1. research capacity, *i.e.* the impact in terms of research ability and skills of the researchers and his/her team;
2. career improvement, *i.e.* the benefits for career and reputation;
3. healthcare benefits, *i.e.* the impact in terms of improvement in diagnosis and treatment skills;
4. knowledge production, *i.e.* the capacity of generating scientific knowledge also considering patenting (including entrepreneurial possibilities) and impact on policy making.

All the variables are described in detail in the Supplementary Material available online. They were chosen based on the available literature on research and biomedical research impact assessment [2, 9], and on studies on economic impact assessment of clinical research organizations and clinical trials [8,16].

The variables concerning the capability of improving health (healthcare benefits) and scientific knowledge (knowledge production) originate from the biomedical research assessment model called “Payback” and on its derivations of “social payback” [3] and “payback to society” [14], which underlined the importance of assessing the impact in terms of “research capability improvement” (Research capacity), considered also as the development of cooperation networks, research technologies and equipment acquisition, training of a new generation of researchers.

The questionnaire was presented informally to OPBG PIs asking their feedback and comments. They strongly suggested to include the improvement of methodological know-how in the variables concerning research capacity. They also suggested to consider career improvement (in terms of remuneration, reputation, networking with other hospitals and biotech companies) as an important variable to be assessed. This suggestion found confirmation in recent literature [15].

The aspect of patenting and entrepreneurial capacity has been inserted in order to open up a subsequent search possibility. In fact, it is assumed that these aspects are evaluated with very low scores, despite the fact that conducting clinical trials is an activity with a high content of industrial innovation. This could be an aspect of further investigation and study, promoting analysis of models capable of stimulating forms of participation by

researchers in industrial development projects. The assessment point concerning policy making responds to one of the most highlighted aspects of scientific research impact analysis. Indeed, many studies note that research produces impact as much as its outcomes are taken into account in terms of public health policy [17].

The questionnaire includes multiple choice questions and ranking questions. No open questions are included. The questionnaire was submitted to the researchers involved in clinical trials at Ospedale Pediatrico Bambino Gesù. Anonymity of respondents was maintained. The list of respondents was provided by the Hospital Research Direction. The total number of respondents is 265.

The questionnaire was administered on-line through the web-based platform Monkey Survey, during March - April 2020. Respondents were reached through an e-mail message containing the rationale of the survey, bibliographic references and a link to the on-line questionnaire. Two reminders were sent by email 15 and 30 days after the first email. To stimulate participation, a number of researchers (one for each research department) were engaged one to one.

Due to the descriptive nature of data, statistical analysis techniques were not used.

RESULTS

As indicated in *Table 1*, the survey target population is made of 265 persons, *i.e.* the healthcare personnel of the IRCCS Ospedale Pediatrico Bambino Gesù who have been involved in at least one clinical trial. Of this target population, 205 subjects took part in the survey. The respondent population is predominantly female (about 60%), and 77% of them are clinicians. The average age is of about 50 years. 43% of respondents have an over 10-year-experience in clinical trials. If we decrease the length of experience to a minimum of 5 years, the percentage rises to 80%. The average age and the length of experience in clinical trials suggest that the trial population can be defined as an “expert group” in clinical trials.

By crossing the clinical trial experience with the professional area of origin, it results that 90% of the population with an over 10-year experience in clinical trials is made of clinicians. Furthermore, 92 % of the surveyed population have been involved in clinical trials outside of Italy for less than 5 years. It is therefore legitimate to consider that the respondent’s group has gained its experience mainly in Italy. Finally, 89% of the population confirmed their involvement in clinical networks. Based on the above results, we may define the respondent population as “a group of clinicians with a consolidated experience in the experimental studies, gained mainly in Italy and with a widespread participation in research networks”.

Concerning the analysis of the four variables, it has been observed that:

a. Research capacity: the distribution of answers to the question on the economic benefit related to the participation in clinical trials is surprising: respondents do not consider as highly significant the economic benefits obtained through their participation in the trials. The most

Table 1
Analysis of the survey respondent population

	Number	Percentage
Category		
Target population	265	
Survey participants	205	
Male	86	42%
Female	119	58%
Job area		
Clinic	124	61%
Surgery	29	14%
Laboratory	17	8%
Research Department	13	6%
Other	23	11%
Job description		
Physicians	157	78%
Sanitary personnel	32	16%
other	13	6%
Years of experience in clinical trials		
1 - 3	43	22%
4 - 6	39	20%
6 - 10	31	15%
More than 10	85	43%
Years of experience abroad		
5 or less than 5	181	92%
6 - 10	14	7%
More than 10	2	1%
Involved in clinical network	178	89%
Experience as Expert Evaluator in international calls	55	28.6%

frequent response is “fairly significant”; more than half of the population (65%) considers the economic impact as not significant (score: 1,2,3. Weighted average: 2.9). Similarly, the additional aspect concerning the benefit in terms of research infrastructure or technologies obtained as a result of the trial, has been considered as not particularly significant (*Figure 1*).

The distribution of answers to the questions concerning the intangible impact of the trials (*i.e.* the impact in terms of increased clinical and methodological know-how and in terms of relational connection in research networks – *Figure 1*) suggest, on the contrary, a highly significant impact (score 4 and 5 for 85% of respondents). As regards the questions on organizational benefits, the majority of respondents considered that their participation in clinical trials significantly improved their involvement in the organizational and information processes of their research organization. Such impact can also be considered as “intangible” since it is a functional benefit consisting in a stronger connection of the researchers and their teams to the organizational flows of the Hospital.

b. Career improvement: as regards the analysis of responses regarding the impact on professional improvement, almost 70% (68%) of the population surveyed considers their participation in trials as significantly important for their professional growth. Among them, one out of four respondents (25%) considers it as extremely relevant to their professional development. These answers need to be interpreted and it seems legitimate to wonder why the population surveyed think that the trials have helped or are helping them in their professional growth. The answer to this question is not related to an increase in reputation or professional prestige within the research organization where the researchers belong, as this aspect is considered as not highly significant by respondents, and certainly less significant than the reputation acquired outside the research organization they belong in. The population surveyed, in fact, seems to believe that participation in the trials has first of all improved the following professional skills (*Figure 1*):

- clinical decision: 32% of respondents believe that participation in clinical trials has significantly increased (rating: 4 out of 5) their diagnose ability and clinical decision-making. This percentage increases to 45% if we consider those who gave the maximum rating (4 and 5) to this question;
- openness towards new therapeutic approaches: 34% of respondents consider that their participation in clinical trials contributed very significantly (rating: 4 out of 5) to the increase of their openness to new therapeutic approaches. This percentage increases to 50% if we consider those who gave the maximum rating (4 and 5) to this question;
- data management: one out of three respondents (33%) considered that participation in clinical trials contributed significantly (rating: 4 out of 5) to the improvement of their abilities in data collection & management. This percentage increases to over 50% if we consider those who gave the maximum rating (4 and 5) to this question;
- data analysis: more than 50% of respondents consider that participation in clinical trials contributed in a significant way (rating: 4 and 5 out of 5) to the improvement of their abilities in data analysis. The ability to analyze, interpret and understand data is the skill, which has received the best rating (highest weighted average rating).

Among the benefits in the professional field, the positive impact on external reputation has been considered as much greater than that on internal reputation. Almost 70% (69%) of respondents rated external reputation 4 and 5 out of 5, thus considering that participation in clinical trials had increased their external visibility, which also resulted in an attractiveness for potential partners and investors. It is the writer's opinion that this external visibility and professional attractiveness may translate into an improvement of scientific reputation, an increase in professional connections and opportunities and consequently also in the improvement of job opportunities and remuneration.

As regards part of the assessment of the impact of participation in clinical trials on careers, *Figure 1* de-

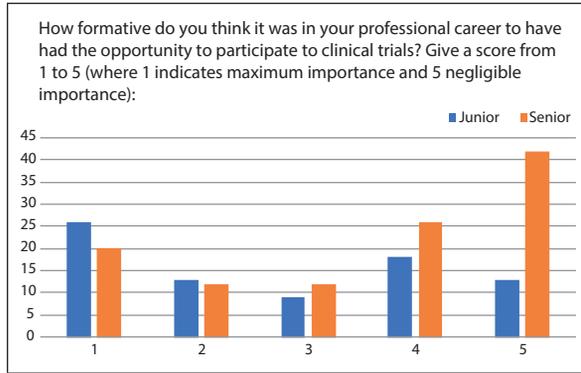


Figure 2

Impact of clinical trial participation on professional career (answers distribution related to years of working experience. Junior: working experience less than 6 years; Senior: more than 6 years).

viewees have, the greater the importance they attach to clinical trials in terms of educational impact. This may be because younger respondents consider the participation in clinical trials as particularly formative.

c. Healthcare benefits: respondents consider the impact of participation in clinical trials on their ability to care and generate health (“Healthcare benefits - health improvements”) as very significant. Understandably and quite predictably, in numerical terms, the variable considered as the most significant was treatment capacity; because trials allow using and administering innovative devices and drugs (score 4 and 5 given by 71% of respondents). However, when comparing the weighted average values (3.88 vs 3.93), ability to diagnose and clinical decision-making seem to be considered as the most significant, as the trial allows acquisition of a higher level of knowledge on the specific condition involved in the trial itself. On the other hand, it should be noted that the scores given to “recruitment capacity” have had the lowest weighted average compared to the other variables of the block “health benefits” (3.64 vs 3.88 and 3.93). The respondents probably consider that participation in clinical trials has a less significant impact (although patient recruitment is inherent in the very nature of clinical trials) on the ability to attract new patients in relation to the condition involved in the clinical trial itself.

d. Knowledge production: impact assessment of participation in clinical trials on the ability to generate scientific knowledge has had different results depending on the areas analyzed. The most significant weight has been found in the scientific production capacity. 70% of respondents gave the highest scores (4 and 5) to this area. There is no doubt, therefore, that participation in trials had an impact on the publication of new scientific papers and on scientific and cultural production in general within the scientific community. Equally, a very important weight was unanimously given to the capacity of innovation: 69% of respondents gave the highest scores (weighted average: 3.84) to “capability in developing new drugs or devices”, which represents the core activity of clinical trials.

A completely different weight was given to the ability to contribute to patenting, which almost 40% of respondents considered as insignificant: almost 60% of the survey population gave a score of 1 and 2 out of 5 to this area. The same applies to the “entrepreneurial” impact: 57% of the survey population seems to believe that participation in clinical trials did not open entrepreneurial opportunities in terms of spin-offs or start-ups.

On average, the impact on involvement in policy-making processes through the production of documents with a regulatory impact or on participation in study commissions or public initiatives at an institutional level has been evaluated as not very significant. One out of four respondents (24.6%) believed that their participation in clinical trials did not give them any role in policymaking processes related to the field of the trial itself.

DISCUSSION

Based on the above data, the following conclusions, summarized in synthetic statements, may be proposed (see below).

Clinical trials mean “better researchers” rather than “higher budget”: the main finding of this survey is that participation in clinical trials increases research capacity. There is almost unanimous agreement that participation in clinical trials produces a significant improvement in the researcher’s level of knowledge about a specific condition, in terms of methodological know-how and available clinical data. Participating in trials also means more connections with research networks and therefore exchange of information and know-how related to a specific condition. The innovative aspect, which would deserve further research, is that this positive impact is considered as greater in an intangible sense than in a tangible one. In other words, the interviewed population believes that clinical trials increased their research capabilities in terms of improved scientific know-how and research connections, more than in terms of available economic resources and infrastructure.

Clinical trials mean “better physicians”: questions on career improvement were asked to analyze the impact of participation in trials in terms of career opportunities. All respondents agree that participation in clinical trials had a positive impact on their careers and improved their professional skills, thanks to a significant development of their diagnosis and clinical decision-making skills, an increased openness towards new therapeutic approaches, and an improved competence in the collection, management and interpretation of clinical data. Considering that the survey population is a “group of experienced physicians”, as previously established, it could be concluded that participation in clinical trials helped them become better doctors. If we also consider the results related to the reputation, we can conclude that participation in trials made them become “better doctors” both in terms of clinical competence and effectiveness and in terms of external reputation and professional prestige.

Clinical trials mean learning opportunities for young researchers: the younger respondents are, the more they feel participating in trials had a strong educational im-

pact. This finding confirms that participation in clinical trials increases clinical and methodological know-how and this is particularly felt by younger researchers.

Reputation and professional prestige emerge as a rather controversial aspect: in fact, the interviewed population considers the improvement of their reputation as researchers more in relation to the external scientific community (and related funding opportunities) than within the professional community of their own institution. This finding may suggest a certain frustration among the surveyed population and it may have implications both for HR Management and Internal Communication policies.

Clinical trials mean "Better care more than better drugs": this conclusion derives from a critical reading of the results on "Health improvement". Clinical research leads to better treatments, not only because it makes available new and potentially more effective drugs, but above all because, according to the interviewed population, they improve clinical decision-making skills. We may therefore conclude that clinical trials lead to better treatment because they help train better doctors, and not only because they provide access to potentially better drugs and devices;

"Patient recruitment as a critical issue": the survey does not explicitly address the issue of patient recruitment, but this aspect emerged quite critically in the context of "Health improvement" questions. The interviewed population believes that participation in clinical trials improved their ability to administer better drugs or use biomedical devices, and that it improved their diagnosis and clinical decision-making skills, but did not as much improve their ability to attract new patients. This is rather surprising, as patient recruiting is a fundamental aspect of clinical trials and one of its success factors. The topic of patient recruitment seems to be a critical issue, which emerged from this survey, even though it is not its focus.

Clinical trials mean scientific knowledge and system: the survey population does not question the fundamentals of "Knowledge production": clinical trials produce new knowledge and new biomedical technologies. The respondent population unanimously agreed on this. This new knowledge is made available to the scientific and health community and strengthens the fundamentals of research. Participating in clinical trials establishes or strengthens professional links and connections with new research groups. Clinical trials, therefore, help develop a "scientific research system".

Clinical trials mean researchers but not entrepreneurs: the low scores given to the impact on patenting or entrepreneurial capabilities need to be further examined also in relation to the so-called third mission of research institutions and universities. In fact, it is now universally recognized that research and academia need to have an important role in technology transfer for the development and promotion of technologies resulting from the research projects they conduct, and more generally, in the management of intellectual property. This survey results are not enough to conduct a comprehensive critical analysis of these aspects, however, our findings suggest a negative perception of

the possibility of being involved in patenting or other business activities. The interviewed population seems to be almost unanimous on the belief that clinical trials today do not open business opportunities to researchers.

Lack of engagement in policymaking: a mode of interaction between the world of research and the society lies on the ability (of research) to improve the general well-being by increasing knowledge, cultural and educational contents and awareness. In this regard, the importance of being involved in policymaking is crucial. The interviewed population considers their contribution to policy making in the field of experimental research to be of little significance. Our survey seems therefore to confirm the lack of dialogue between researchers and policy makers. This aspect calls for a reflection on the opportunity to involve researchers engaged in clinical trials in institutional forums, as well as on the ability of research institutions to present the results achieved in political settings. The importance of the use of health research in policy-making, and of understanding the mechanisms involved, is increasingly recognized. Recent reports calling for more resources to improve health in developing countries, and global pressures for accountability, draw greater attention to research-informed policy-making [18]. The utilisation of health research in policy-making should contribute to policies that may eventually lead to desired outcomes, including health gains [19].

CONCLUSION

The aim of this study was to give a contribution to the debate on the economic and cultural impact of clinical trials on the society. The main variables and methods to assess the social impact of biomedical research have been used [20]. A survey was administered to a population of researchers to assess impact under a different perspective.

The choice of the IRCCS Ospedale Pediatrico Bambino Gesù is motivated by the specific experience of this Hospital, the largest children's hospital in Europe and one of the largest in the world, which makes it particularly adequate to the aims of this study [21]. OPBG is in fact one of the most attractive facilities in terms of paediatric clinical research, with a high number of researchers and of ongoing clinical trials [22].

The choice to administer the questionnaire to a limited population is a limit of this study, but it opens the possibility to replicate it to a more extensive population, e.g. the entire group of the so called IRCCS (Italian biomedical Research Hospitals), which have different legal natures, operate within different biomedical and clinical research areas, and have different geographical positions. Such an extension of the study would make it more comprehensive, robust and with a national perspective. Another limit is that the method of impact assessment does not consider the different research areas. In fact, researchers on different research areas may evaluate differently the impact of their participation in trials. A possible development of this study could therefore also consider the differences in the assessment following the different research ar-

eas. Recent literature has showed that hospital management has a low awareness of the benefits clinical trials provide to hospitals [7, 8, 23]. In this regard, another limit of this study is that managers have not been included in the survey.

The above discussion leads to new questions. For example, considering the benefits that researchers recognize in their participation in clinical trials, it is legitimate to wonder how much research institutions encourage and enhance researchers' participation in trials. From another point of view, the interviewed researchers consider the "cultural" benefits more important than the economic and infrastructural benefits. It would therefore be interesting to see which are the policies and instruments research centers activate to make participation in trials more economically meaningful. In addition, new policies would be needed to allow researchers' direct access to funds for entrepreneurial development related to their research. Our survey results also suggest that there are communication issues: internal communication within the research center, external communications towards patients (for recruiting purposes), communication between research groups and health policy makers (in order to bridge the gap between science and policymaking [24]).

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Rubella immunity status and the active offer of MMR/MMRV vaccination during pregnancy

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Abstract

Introduction. The rubella test during pregnancy makes it possible to identify situations at risk of congenital rubella and those pregnant mothers who should be offered the MMR vaccine.

Materials and methods. The Authors analysed test coverage and the immunity status of pregnant mothers between 2005 and 2017, using birth attendance certificates.

Results. Rubella test coverage on 61,437 pregnant mothers was 99.4%. The average proportion of susceptible subjects was 6.4%. Seroconversion was observed in 7 cases, with 1 confirmed case of congenital rubella. 32% of susceptible subjects were vaccinated, and adherence was seen to be influenced by the characteristics of the pregnant women and of the maternity unit.

Conclusions. A current information flow including a number of healthcare services, is useful both for monitoring the maternity care pathway and for public health purposes.

Key words

- rubella
- rubella test
- pregnancy
- congenital rubella
- MMR/MMRV vaccine

INTRODUCTION

In line with the guidance provided by the WHO's European Region, the Italian National measles and rubella elimination plan that was approved in 2003 set the goal of eliminating the endogenous transmission of measles and of reducing the incidence of congenital rubella to less than 1 case/100,000 live births, by 2007 [1].

The consequent review of the national vaccination calendar provided, for all new births, for a first dose of trivalent vaccine (MMR: Measles-Mumps-Rubella) within the first 15 months of life, followed by a second dose at 5-6 years of age. It also envisaged the recovery of vaccination coverage amongst adolescents and women of childbearing potential. Amongst this latter population, the aim was to reduce the proportion of susceptible women to under 5%. As the first edition of the plan did not meet the targets set, the objectives of the second National plan for the elimination of measles and congenital rubella (2010-2015) also included interrupting the endogenous transmission of rubella [2]. The approaches used to provide MMR vaccination were

also confirmed by the most recent review of the Italian National Vaccination Plan [3].

The recent ministerial circulars on recommended vaccination for childbearing and pregnant women, (8.7.2018, 11.12.2018, 11.21.2019) recommend evaluating the immune status of the pregnant women also with respect to chickenpox, actively proposing, where necessary, also the MMRV vaccination [4].

The action taken in response to the WHO's guidance also varied both between European countries [5], and between the individual regions of Italy [6].

In 2005, a study was initiated in the province of Trento (north-eastern Italy, population of 540,000 inhabitants as at 1.1.2018), to monitor the specific immunity status amongst pregnant women, by gathering data on the results of the rubella test performed during pregnancy from birth attendance certificates. Birth attendance certificates constitute the primary source of information on births, antenatal care and childbirth and must be compiled by law throughout Italy by the healthcare professional (usually a midwife) who was present during childbirth [7]. The birth attendance

certificate used in the province of Trento also records any MMR/MMRV or monovalent rubella vaccination, which is actively offered in all maternity units, after the birth, as part of a programme established with the Provincial Health Service's Department of Prevention, and as such already included in the first provincial prevention plan for 2007-2009 [8].

This paper reports on the trends for rubella test coverage and for the immunity status of pregnant women receiving care in maternity units within the province of Trento between 2005 and 2017, together with the trend regarding the proportion of non-immune mothers who were vaccinated after giving birth and prior to discharge, and the trend regarding the health of babies whose mothers seroconverted during pregnancy.

MATERIALS AND METHODS

The birth attendance certificate used in the province of Trento includes a far greater number of variables than the national Ministry of Health template. In addition to other variables, it also collects information regarding infections during pregnancy and, in particular, data regarding serological screening tests. These include the results of the rubella test performed to analyse the susceptibility of pregnant women to rubella virus infection.

The diagnostic kit used at the Microbiology Unit of S. Chiara Hospital of Trento, which acts as the hub centre for the entire province is Abbott's Rubella IgG/IgM Reagent Kit that uses chemoluminescent immunological technology to capture microparticles. The cut-offs used to define positivity for IgG and IgM are respectively 10.0 UI/ml and 1.60 index. Each positive value is subjected to confirmation test. The determination of the avidity of the IgG is expected, for the dating of the infection. A high IgG avidity (over 20%), indicates a previous infection (more than three months before the date of the test).

The rubella test is part of the screening programme provided to guarantee an adequate monitoring of pregnancy and as such does not involve any co-payment by users. The test is performed in the early weeks of pregnancy and in the case of confirmation of immunity (positive specific IgG with negative specific IgM), prior illness or prior vaccination, it is not repeated. In the presence of a state of susceptibility (IgG and IgM negative), the test is repeated every 4-6 weeks, until at least the 5th month [9].

From 2005, as part of a joint project with the Department of Prevention, the Clinical and Evaluational Epidemiology Service, which also manages all information flows regarding the maternity and paediatric areas, included in birth attendance certificate, which are recorded on electronic storage devices at each maternity unit, not only the result of the rubella test, but also any MMRV/monovalent rubella vaccine administered to the mother. This activity, which is supervised by the same midwives who were present during childbirth, was introduced after an information/ training phase that, at various timepoints, involved all professionals working in the province's maternity wards, which during the study period decreased from 8 in 2005 to 4 in 2018. The flow chart with the time line of all the interventions and the number of pregnant women involved is shown in *Figure 1*.

The vaccine is offered to pregnant women with a negative or ambiguous rubella test result, usually on the second day after childbirth or on the day of discharge. The healthcare professionals collect a preliminary pre-vaccination history, using a standard template compiled by the Department of Prevention, and usually offer women the trivalent MMR/MMRV vaccine, which can be replaced with the monovalent rubella vaccine, if requested by the woman.

The maternity units regularly send the MMR/MMRV monovalent rubella vaccination certificates to the

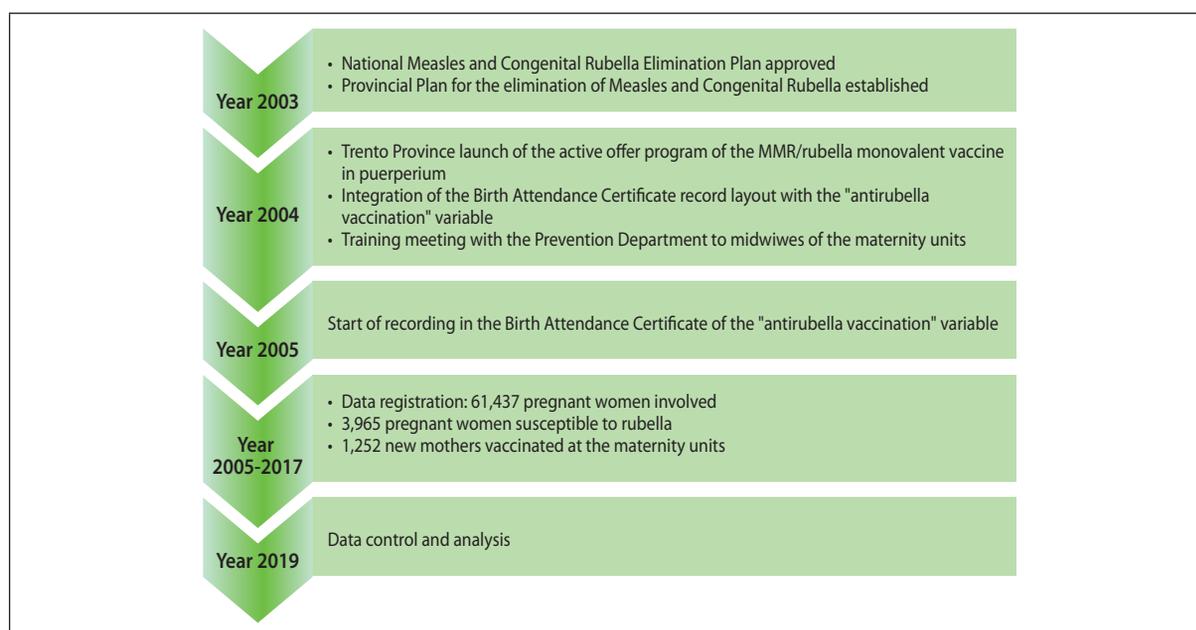


Figure 1
Flow chart of the interventions and women participating.

competent local vaccination services. The certificate includes the name, surname and date of birth of the mother and her child and the vaccine's identification data (batch number, expiry date, etc.). Cases of refusal are also reported, so that vaccination service staff can record it on the baby's electronic vaccination record and offer the mother vaccination when the baby has his/her first vaccination.

In cases of voluntary termination of pregnancy, the healthcare professionals working at the Obstetrics and Gynaecology Unit advise women who are not sure they are protected to have MMR/MMRV or monovalent rubella immunisation at their local vaccination service clinic.

The data that were missing from the birth attendance certificate database regarding the rubella test results or vaccination were retrieved retrospectively by the Clinical and Evaluational Epidemiology Service by accessing the Hospital Information System, which contains all the results of user contacts with the provincial health services. For women who seroconverted, it was also necessary to access the Hospital Information System to ascertain at what point of the pregnancy the rubella test was found to be positive.

Between 2005 and 2017, the birth attendance certificate database was used to analyse the proportion of pregnant women who had the rubella test of those receiving care at the maternity units in the province and, therefore, the trend for immunity to the rubella virus. We also analysed the time trend of the proportion of non-immune mothers who were administered MMR/MMRV/monovalent rubella vaccine after giving birth. The data regarding the rubella test and immunisation were analysed considering, on the one hand, the characteristics of the maternity unit and, on the other, the characteristics of the mothers, more specifically, their nationality (Italian vs. other nationalities), age range, parity and academic qualifications. The factors associated with adherence with the offer of post-natal immunisation were analysed by multiple analysis using the logistic regression model in which the explanatory variables were age range, nationality (Italian vs other), academic qualifications, marital status, parity and the maternity unit. Babies whose mothers seroconverted during pregnancy were evaluated to establish their state of health, using the information present in both the Hospital Information System and Hospital Discharge Records, by extracting records with a "7710" code for both the first diagnosis and subsequent co-diagnoses. Trend significance was analysed using the Cochran-Armitage test for trend and the significance of the differences between the proportions was analysed using the chi squared test or Fisher's exact test. The statistical analyses were performed using Epi-Info software.

RESULTS

Between 01.01.2005 and 31.12.2017, 61,437 pregnant women received care at hospital maternity units in the province of Trento, with an annual average of 4,720 and a total number of 62,275 live births during the observation period. The overall average age of the pregnant women rose from 31.2 years in 2005 to 32 years

in 2017; amongst Italian women the average age was higher than amongst foreign women and rose from 32.6 years in 2005 to 33 years in 2017. The modal age range was that between 30 and 34 years, which accounted for 34.7% of all the pregnant women considered during the study period. 23.7% of the total were foreign women, with a proportion that increased over time from 18.7% in 2005 to 26.2% in 2017; 95% of the pregnant women considered during the study period were resident in the province of Trento.

Considering the entire study period, 99.4% of all pregnant women had a rubella test, with a coverage that ranged from 98.8% in 2005 to 99.9% in 2017. Practically all of the pregnant women had a serological rubella test, with a slightly (not statistically significant) lower coverage rate in mothers aged 15-18 years (97.5%) and in those residing outside the province (97.8%). No statistically significant differences were observed in the serological results between Italian women (99.7%) and women of other nationalities (99.2%), or with regard to parity or academic qualifications. Lastly, there was no difference in rubella test coverage with regard to the maternity ward, with coverage that ranges from 98.7% to 99.9%.

The immunity status of the pregnant women undergoing serological testing during the study period (61,103 subjects) is shown in *Table 1*. A certain non-homogeneity can be observed regarding age range (*Table 2*), where the proportion of susceptible subjects is higher than expected, in a statistically significant manner ($p < 0.001$), in the <25 years age ranges and decreases with an increase in age, with a statistically significant trend ($p < 0.01$).

Table 1

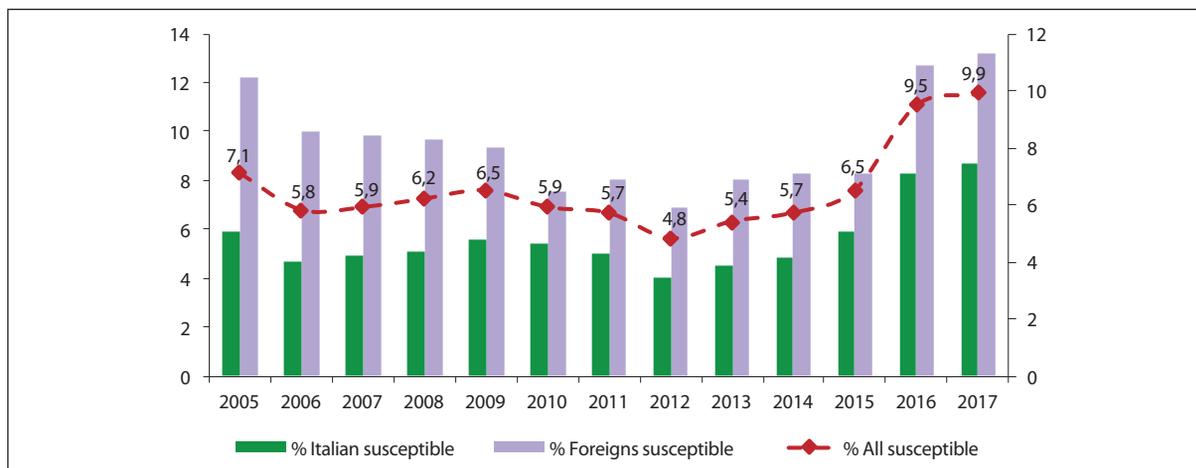
Province of Trento. Immunity status of women undergoing the rubella test during pregnancy receiving care in the province's maternity units. Period: 2005-2017

Immunity status	Frequency	%
Susceptible	3,965	6.49
Immune	57,131	93.50
Seroconversion during pregnancy	7	0.01
Total	61,103	100.00

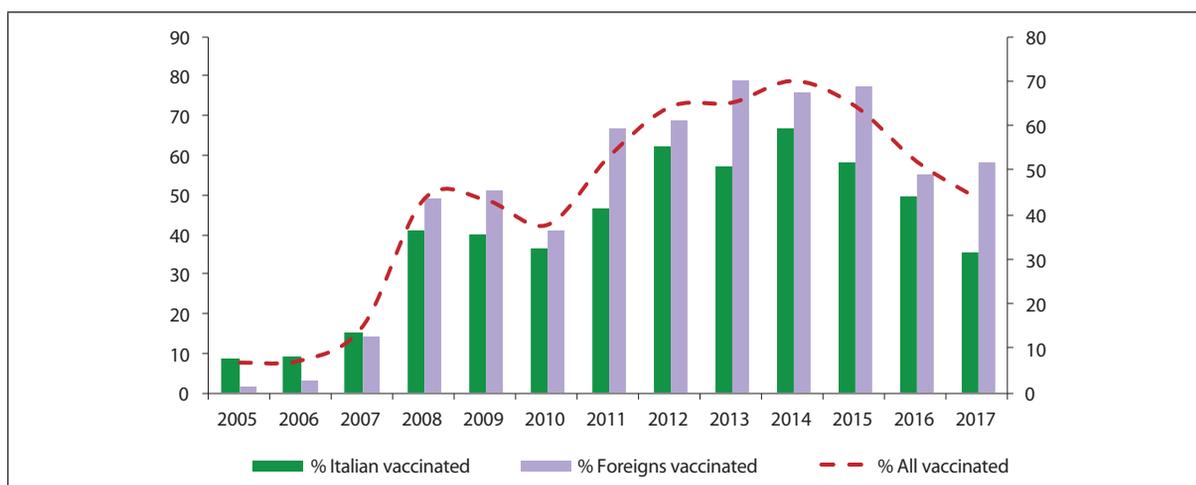
Table 2

Province of Trento. Proportion of subjects susceptible to rubella by age range in women undergoing the rubella test during pregnancy receiving care in the province's maternity units. Period: 2005-2017

Age range	% susceptible to rubella
15-18	14.5
19-24	9.4
25-29	7.8
30-34	5.7
35-39	5.2
40+	5.1

**Figure 2**

Province of Trento. Annual proportion of women susceptible to rubella infection amongst women receiving care in the province's maternity units. All pregnant and pregnant grouped by nationality. Trend for 2005-2017

**Figure 3**

Province of Trento. Annual proportion of women susceptible to rubella infection vaccinated against rubella in the province's maternity units. All pregnant and pregnant grouped by nationality. Trend for 2005-2017

The proportion of susceptible women, which was on average equal to 6.4%, increased from 7.1% in 2005 to 9.9% in 2017 (Figure 2), with an increase that, overall, was not statistically significant. This increase is only statistically significant amongst pregnant women under 24 years of age, in whom it rose from 18% in 2005 to 30% in 2017. The proportion of susceptible women remains higher in each year among foreign women than Italians (9.4% vs 5.5% for the entire period), and this difference was statistically significant ($p < 0.001$). No other difference was observed with regard to parity or academic qualifications.

Of the 11 women, who "seroconverted during pregnancy" as recorded on the birth attendance certificate, just 7 were confirmed as having seroconverted by the data in hospital discharge records, due to recording errors at the maternity ward. There were therefore effectively 7 women who seroconverted during pregnancy, of whom 5 were foreign and 2 were Italian, for an overall seroconversion rate of 0.11/1000 and a sero-

conversion rate of 0.34/1000 amongst women of other nationalities and 0.042/1000 amongst Italian women. The seroconversion rate was seen to be 8 times higher amongst foreign women than amongst Italian women. In the cohort of pregnant women included in this study, there was just one case of congenital rubella, following infection of the mother (of Romanian origin) confirmed around the 15th week of gestation. The child was found to have a significant psychomotor retardation and hearing loss.

In all, 1,252 women were administered MMR/MMRV or monovalent rubella vaccine in the province's maternity units, equal to 31.6% of susceptible subjects. The proportion of vaccinated subjects followed an increasing trend over time (Figure 3), and this trend would appear to be statistically significant ($p < 0.01$) despite undergoing a certain drop in the last three years of the study. Vaccines were administered to 27.2% of susceptible Italian women and 38.3% of susceptible women of other nationalities, with a statistically significant differ-

ence in favour of foreign women ($p < 0.001$). The characteristics of susceptible women according to the adherence to the vaccination offer and the factors associated with adhering to the vaccination offer are reported in Table 3. Young age at childbirth (< 24 years), a primiparous condition, and foreign nationality were the independent personal characteristics that were most statistically significantly associated with adherence with the offer of rubella immunisation. Childbirth at a maternity unit with approximately 500 births a year or less was another factor seen to be associated with vaccination adherence. When all other conditions were equal, marital status and academic qualifications did not appear to affect vaccination adherence.

DISCUSSION

Serological determination of the specific IgG antibody titre during the first antenatal consultation in order to evaluate immunity to the rubella virus and the consequent need for immunisation in the post-partum period is the most common screening strategy in developed countries, with coverage levels of approximately 90-95% [10].

The use of a current information flow such as the birth attendance certificate database in order to monitor the presence of infections during pregnancy can prove convenient, despite being demanding for the ma-

ternity unit professionals who, amongst other things, have to retrieve, check and record the pertinent data. Use of this approach also appears to be limited in Italy, where experiences have only been recorded, at least to the authors' knowledge, in the province of Trento and the Emilia-Romagna region [6].

The information obtained using this approach makes it possible to obtain an overview of the whole population considered, rather than of a specific facility. This undoubtedly brings advantages in terms of data bias over studies based on samples from a single facility [11-15]. The data extrapolated from birth attendance certificates nevertheless require a certain amount of cross-checking with other sources, such as hospital information systems, especially when data are missing or inaccurate, or in the case of prospective data, such as those regarding babies whose mothers seroconverted, whose subsequent health status cannot be defined by birth attendance certificates alone. Birth attendance certificates can nevertheless prove to be useful for monitoring a specific public health initiative, such as offering rubella immunisation to susceptible pregnant women, which is one of the cornerstones of the prevention of congenital rubella syndrome and as such is recommended by the WHO [16].

The rubella test is performed in practically all of the pregnant women receiving care at the maternity units

Table 3

Province of Trento. Characteristics of pregnant women susceptible to rubella infection and their adherence to the immunization offer (absolute numbers, percentage, multivariate adjusted odds ratio and 95% confidence intervals). Period: 2005-2017

Characteristics	Susceptible		Vaccinated		Multivariate Analysis	
	N	%	N	%	Odds Ratio	95% C.I.
	3965		1.252	31.6		
Maternity units (MU) by number of births per year						
MU with <500 births	1594	39.6	396	24.8	1.80	1.53-2.12
MU with 500-1000 births	894	22.4	327	36.5	0.92	0.77-1.10
MU with >1000 births	1477	37.1	529	35.8	1	
Age class						
<=24 y	566	14.1	244	43.2	1.29	1.01-1.66
25-29 y	1053	26.4	358	34.8	1.18	0.95-1.46
30+ y	2346	59.0	650	27.7	1	
Citizenship						
Foreigners	1390	34.8	551	39.6	1.82	1.55-2.12
Italian	2575	64.8	701	27.2	1	
Marital status						
Married	2659	66.9	820	30.8	1.08	0.92-1.28
Unmarried	1149	28.9	392	34.1	1	
Other	157	3.9	40	25.5	1.14	0.76-1.70
Education						
Primary school/no education	140	3.5	58	41.4	0.78	0.52-1.15
Lower secondary school	987	24.8	283	28.7	1.14	0.92-1.42
Upper secondary school	1980	49.8	645	32.6	0.89	0.74-1.07
University degree	858	21.5	266	31.0	1	
Parity						
Primiparous	2006	50.5	755	37.6	1.72	1.47-2.01
Pluriparous	1959	49.2	497	25.4	1	

Note: in the multivariate analysis, the reference category is the one with the odds ratio=1 and the bold character indicates a p value less than 0.05.

in the province of Trento, without any relevant variations from one year to another, with values that would appear to be higher than those reported in other regions of Italy [6]. The level of rubella test coverage does not vary with maternal characteristics such as academic qualifications and parity and only appears to be slightly lower amongst the younger age ranges and those living outside the province. No inequalities were observed in the access to or use of the test with regard to nationality, neither was there any non-homogeneity with regard to the maternity units or health districts attended by women living in the province. This demonstrates the homogeneity and equality of the management of maternity care throughout the area. The average proportion of susceptible women for the whole study period was 6.5%, which is lower than reported in prior Italian studies [6], but substantially in line with studies conducted in other European [17] and Asiatic [18, 19] countries.

The proportion of susceptible subjects would appear to be higher amongst younger women of up to 24 years of age, as reported in previous studies [19-24] and this sub-population underwent an increase in susceptible women over time, most likely due to a reduction in immunisation adherence during childhood and adolescence. Our results confirmed that the proportion of susceptible subjects is higher amongst foreign women [12, 13; 20-22], a fact that must be taken into due consideration in view of the increase in various areas of the country in the number of foreign women of childbearing potential associated with migratory processes. Overall, the proportion of susceptible pregnant women is still above both national and international targets [2, 3].

Although the seroconversion rate was very low, it was nevertheless 8 times higher in foreign women than amongst Italian women [10]. The retrospective assessment of babies born to mothers who seroconverted revealed, over a long period of time, just one case of congenital rubella, equal to 1.5/100,000 live births, a value that exceeds the national value provided by the surveillance system for congenital rubella and rubella during pregnancy [25].

Almost 1,250 women were immunised after giving birth, equal to an average of 31.6% of susceptible subjects, over the entire study period, with an increasing trend up to 2014 that was followed by a decrease, possibly due to the expansion of the anti-vaccination movements that had a certain impact, even locally. Offering MMR/MMRV/monovalent rubella immunisation in the postnatal period is a good opportunity for increasing vaccine coverage, if we consider that each user contact with the health services could provide an opportunity to offer an effective prevention practice [26, 27]. This

specific action, which must be combined with the vaccination campaign address the general population, would appear to be both feasible and sustainable, within the context of a strong interaction between the various provincial healthcare services. Nevertheless, it is necessary to question the validity of the level of vaccination adherence achieved, considering that the level of adherence presents a dual stratification in accordance with maternal characteristics and maternity ward characteristics. As far as maternal characteristics are concerned, foreign mothers, primiparous mothers and younger mothers show better adherence with the offer of immunisation. With regard to the characteristics of the maternity unit, vaccination adherence is higher in maternity wards with a lower number of births. This may be due not only to greater staff sensitivity, but also to the fact that healthcare professionals in smaller maternity units have fewer time restraints. This may facilitate communication between healthcare professional and user/patient, as postulated in previous Italian studies [28, 29]. It could be useful to analyse the barriers to vaccination perceived by mothers, in order to adjust the criteria and approach used to propose MMR/ monovalent rubella vaccination in the post-partum period [30].

CONCLUSIONS

It is essential to continue monitoring access to the rubella test and seroconversion during pregnancy in the context of better interaction between maternity unit, the department of prevention and the epidemiology service, as we are still far from the targets set. Current information flows that are suitably combined with other data sources to meet the user's needs are extremely useful not only for monitoring maternity care, but also for analysing the process and outcome data of a public health initiative. The routinely collected data nevertheless require a certain degree of quality control, especially for a precise definition of seroconversion and the analysis of the neonate outcomes. In this perspective, the possibility of accessing hospital information systems would appear to be very useful, without being particularly time-consuming, at least on a local level. It will be necessary to analyse the long-term outcomes of offering MMR/MMRV monovalent rubella immunisation in the postnatal period, in order to establish to what extent it improves vaccination coverage in women of childbearing potential.

Conflict of interest statement

The Authors report no conflicts of interest.

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First evidence of *bla*_{NDM-1} and *bla*_{OXA-23} carbapenemase genes in human body lice infesting a second-hand T-shirt in a street market in Italy

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Abstract

Background. The spread of carbapenems resistance is a public health concern. The main group of carbapenemases encoding the β-lactamases activity (*bla* genes) is the Metallo-β-lactamases (MBLs).

Methods. The presence of carbapenemase *bla*_{OXA-23-like}, *bla*_{OXA-40-like}, *bla*_{OXA-51-like}, *bla*_{OXA-58-like} and *bla*_{NDM-1} genes was screened by real time PCR in 26 *Pediculus humanus* insects identified from second-hand clothes in a local market in Central Italy. Bacteria diversity was also characterized through shotgun metagenomic amplification for a deep sequencing of the host-associated bacterial microbiomes.

Results. The *bla*_{OXA-23} and *bla*_{NDM-1} carbapenemases genes were found and metagenomic analysis showed a great presence of *Acinetobacter* species.

Conclusions. These results suggest a new potential transmission path for carbapenemase gene spread through bacteria ingested by insects infesting humans.

Key words

- *Acinetobacter* spp.
- *Pediculus humanus*
- NDM-1
- OXA
- carbapenem resistance
- Italy

INTRODUCTION

In recent years, infections attributable to carbapenem resistance gram-negative bacteria have increased and, in many cases, have been associated with high morbidity and mortality rates, due to their extensive antibiotic resistance, extremely difficult to treat [1]. The spread of carbapenems resistant Enterobacteriaceae (CRE) and of carbapenem-resistant *Acinetobacter baumannii* (CRAB) has become a major public health concern. In particular, *A. baumannii* may cause health-care-associated infections worldwide with multidrug-resistant clonal lineage, while community-acquired infections are related to sporadic cases [2, 3]. CRAB and CRE are included in the World Health Organization (WHO) priority list of antibiotic-resistance bacteria to direct future research and development, after an assessment of their importance in both health-care-associated infections and community-acquired infections [1]. Carbapenem resistance was firstly detected in 1990s in *A. baumannii* reporting carbapenemases of class D oxacillinases (OXA), including OXA-23-like, OXA-40-

like, OXA-51-like, and OXA-58-like enzymes [4, 5]. One of the main groups of carbapenemases encoding the β-lactamases activity (*bla* genes) is the Metallo-β-lactamases (MBLs), given its unavailability of commercial MBLs inhibitors, and despite the remarkable research in new drugs development [6]. MBLs of clinical importance are IMP (Imipenem MBLs), VIM (Verona integron-encoded MBLs), SPM (São Paulo MBL), and NDM (New-Delhi MBL) families. The *bla*_{NDM-1} genetic element was identified in 2008 in an Indian patient colonized by *Klebsiella pneumoniae* carrying *bla*_{NDM-1}. The horizontal gene transfer allowed a rapid spread worldwide, among different species circulating in community healthcare and in environmental settings [5, 6]. Several species belonging to the *A. baumannii*-*A. calcoaceticus* complex have been also identified in arthropods (*Pediculus humanus*, ticks and fleas), that are potential vectors for infection transmission [7, 8]. In Italy, only imported cases of louse borne diseases were described and exclusively, in refugees from endemic countries, while autochthonous body louse vectors were considered ex-

tinct [9]. Recently, we have searched body lice found on a second-hand T-shirt bought in a street market near Rome (Central Italy) for *Borrelia recurrentis* (relapsing fever), *Rickettsia prowazekii* (epidemic typhus), *Bartonella quintana* (trench fever), *Coxiella burnetii* (Q fever) and *Yersinia pestis* (plague), with negative results [10].

Here, we report the presence of bla_{OXA} and bla_{NDM-1} resistance genes in lice collected from second-hand clothes in Italy. The metagenomic bacterial species investigation has been also performed.

METHODS

In a collection of 26 *Pediculus humanus* insects identified from second-hand clothes in 2018 in a street market, the presence of carbapenemases encoded by $bla_{OXA-23-like}$, $bla_{OXA-40-like}$, $bla_{OXA-51-like}$, $bla_{OXA-58-like}$, and bla_{NDM-1} genes was detected by PCR using primers as previously described and amplicons were fully sequenced [11].

Species diversity was characterized through shotgun metagenomic amplification for a deep sequencing of the host-associated bacterial microbiomes. A metagenomic analysis of V3–V4 region of 16S rRNA gene was performed by Illumina MiSeq platform (Illumina, San Diego, CA) to better understand the relative abundance of the main bacterial phylum and genus in lice containing carbapenemase elements. Tags and taxonomic annotations from obtained sequences, were calculated with a high level of accuracy (99%), using a combination of specific databases. Raw data were trimmed in quality and normalized. The operational taxonomic units (OTUs) were clustered before taxonomic assignment. Taxonomic information was calculated and summarized.

Acinetobacter species was investigated by real time PCR using primers and probe targeting the *rpoB* gene, and amplicons were examined by nucleotide sequence [12].

RESULTS

Carbapenemase genes were identified in 7 out of 26 (24%) different *Pediculus*. The most relevant results were: 2 lice positive for $bla_{OXA-23-like}$, 2 lice for $bla_{OXA-58-like}$, 2 *Pediculus* for bla_{NDM-1} , 1 *Pediculus* showing a combination of $bla_{OXA-23-like}$, $bla_{OXA-58-like}$, bla_{NDM-1} . No positivity was

found for $bla_{OXA-40-like}$ and $bla_{OXA-51-like}$ genes. Sequences of PCR generated amplicons displayed a 100% identity with GenBank references: $bla_{OXA-23-like}$ (CP042841), $bla_{OXA-58-like}$ (KF700121), bla_{NDM-1} (CP043053).

Lice carrying bla_{NDM-1} element were considered for microbiome bacterial composition. The analysis was assessed at phylum and genus levels and the taxa composed of more than 3% were considered, with a total of usable sequences classified into 8 phyla.

As presented in Table 1, the majority of the obtained operational taxonomic units (OTUs) belonged to Moraxellaceae (30%-60%, *Acinetobacter*), Burkholderiaceae (9%-15%, *Delftia*), Rhizobiaceae (4%-11%), Enterobacteriaceae (3%-13%), Xanthomonadaceae (3%-6%), Flavobacteriaceae (3%-4%), and Pseudomonadaceae (0%-14%).

Acinetobacter spp. were the most represented species and were detected in all lice containing bla_{NDM-1} genes and in 24 out of 26 (92%) of collected insects. Nucleotide sequences of *rpoB* (zone1) genes were compared with the GenBank database sequences, revealing the existence of different species of *Acinetobacter* non-*baumannii*, as *A. ursingii* (accession number EF611406 with 100% identity), *A. pittii* (accession number CP014477 with 100% identity), and *A. johnsonii* (accession number CP037424 with 100% identity).

DISCUSSION

Carbapenem antimicrobial resistance is a public-health problem of global dimension, especially because it is largely found in Gram-negative pathogens. The characteristic gene transfer pathway confers a rapid spreading, causing serious outbreaks and a limited treatment option. To date, in healthcare facilities and within the community, the exact prevalence of carbapenemase-producing Enterobacteriaceae and of carbapenem-resistant *A. baumannii*, is still unknown [1, 4].

Head louse infestation is very common worldwide, with a close head-to-head contact transmission, while the body louse infestation is less frequent and related to poor hygiene. Lice may carry a broad spectrum of pathogens, including Enterobacteriaceae and *Acinetobacter* spp., and acquire these bacteria during blood meals from infected patients. The transmission of these

Table 1
Metagenomic analysis of 3 body louse carrying bla_{NDM-1} element

Family/genus	Body louse carrying bla_{NDM-1}	Body louse carrying bla_{NDM-1}	Body louse carrying $bla_{OXA23-like}$, $bla_{OXA58-like}$, bla_{NDM-1}
Moraxellaceae/ <i>Acinetobacter</i>	60%	39%	55%
Burkholderiaceae/ <i>Delftia</i>	11%	9.0%	15%
Xanthomonadaceae/ <i>Stenotrophomonas</i>	5.0%	3.0%	6.0%
Flavobacteriaceae/ <i>Flavobacterium</i>	3.0%	4.0%	4.0%
Rhizobiaceae/ <i>Ochrobactrum</i>	0.0%	11%	4.0%
Other Rhizobiaceae	6.0%	0.0%	4.0%
Enterobacteriaceae/ <i>Candidatus Riesia</i>	5.0%	13%	3.0%
Pseudomonadaceae/ <i>Pseudomonas</i>	0.0%	14%	0.0%
Others	10%	7.0%	9.0%

microorganisms within the community could occur through the insect feces or by scratching of the skin [13].

The prevention for reducing person-to-person transmission of CRE is a WHO priority [1].

In this study we found different bacterial species in lice implicated in carbapenem antimicrobial resistance. The large presence of *Acinetobacter* leads to speculate an association of these species with the carbapenemase resistance determinants. The detection of *bla*_{OXA-23-like}, *bla*_{OXA-58-like} and *bla*_{NDM-1} genes in body lice, containing a broad range of bacterial species, suggest a relationship with all identified bacteria, especially with Enterobacteriaceae, found in metagenomic analysis. As described by several authors, *Acinetobacter* strains were found in body and head lice, but their clinical implication is still unknown and the vector competence for the maintenance and transmission of those pathogens is not established [8, 13-15].

A high prevalence of *Acinetobacter* species DNA carriage (40.8%), mostly *A. baumannii* (32.9%), in clothes lice collected in 2013-2018 period was observed, tending to increase over time [16]. Moreover, our presented data showed an uncommon finding of different bacterial species, possibly associated to carbapenemase resistance in lice. In particular we found *bla*_{OXA-23-like}, *bla*_{OXA-58-like} and *bla*_{NDM-1} carbapenemase elements. The *bla*_{OXA-23-like} gene encoding the OXA-23 carbapenemase is widespread in clinical isolates and derives from the chromosome of *Acinetobacter radioresistens*, representing an intrinsic gene [17, 18]. The *bla*_{OXA-58-like} and *bla*_{NDM-1} are the most frequently variants found in *Acinetobacter* species [6, 17, 19]. Further studies are required to bet-

ter understand the potential transmission of pathogens carrying carbapenemase genes from vectors to humans, including the possibilities to grow bacteria present in these insects for direct association of these resistance determinants and bacterial species. Greater attention is due to extra-hospital reservoirs of these opportunistic drug-resistant bacteria and their potential involvement in emerging human community-acquired infections.

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Authors' contributions

FM: performed molecular methods and data analyses; LV and AC: analyzed genomic data and revised the manuscript; MM, MDL LT, CL, AM and FR: provided samples and insect data and gave input into the study design; AC: conceived the study, coordinate the study and wrote the manuscript. All authors read and approved the manuscript.

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NEW PERSPECTIVES IN PERINATAL MENTAL HEALTH MODELS: FACING CHALLENGE FOR ITALIAN HEALTH SERVICES

Edited by Gabriella Palumbo, Laura Camoni and Antonella Gigantesco

Preface

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This collection of papers on services for perinatal anxiety and depression are timely and important. It is now well established that perinatal mental health is as important for family and societal well-being as physical health and, as the paper by Vichi and colleagues on suicide reminds us in an excellent review of the topic, it is also one of the leading causes of maternal death in high income countries.

Milgrom and Gemmill have carried out groundbreaking work at the Australian Parent Infant Research Institute (PIRI), developing and evaluating interventions for mothers with perinatal depression based on biopsychosocial approach and tailored for the perinatal period with additional support for the mother infant relationship. Hirshler *et al.* describe the current state of the art services in Australia which includes nationwide screening for perinatal depression and psychosocial risk factors, with both face to face and online screening and intervention programmes. The Australian team had enabled access to include women living in rural settings or with child care needs through their online interventions and they were therefore ideally placed to offer such interventions during a pandemic.

In recent years Italian services had started to implement these approaches in the different settings across Italy, ensuring a range of healthcare providers were included in the training initiatives of these programmes, empowering families with information, and offering assessment and treatment using the PIRI approach which has been found to be effective in the Italian setting. Camoni *et al.* provide a review of these service developments, and also helpfully describe the challenges in implementation and how to address them – for example, through education to address stigma and false beliefs about maternal mental health problems.

Since the Covid-19 pandemic struck in Italy as elsewhere, mental health services changed dramatically, with few face-to-face healthcare contacts other than in emergency situations. As Camoni *et al.* describe,

there is growing evidence, including in Italy, that during the pandemic (and other emergencies), women in the perinatal period have been at increased risk of perinatal depression and anxiety due at least in part to isolation, increases in family violence and alcohol use in the home, and decreased social support. Perinatal mental health programmes have therefore evolved to provide information and screening remotely in addition to face-to-face contacts when on hospital wards or at essential visits to professionals such as paediatricians; then when needed, remote delivery of the CBT intervention developed at PIRI has been provided, both in groups and individually, including intervention focussed on the mother infant relationship. When severe mental illness occurs then face to face assessment and treatment must be available of course, with appropriate physical distancing, personal protective equipment etc in psychiatric facilities or in the home. We have seen in the recent UK Confidential Enquiry into maternal suicides that failure to assess high risk cases face to face may lead to an increased risk of suicide [1].

The modifications to care described here have been an essential component of perinatal mental health care in 2020 and I have no doubt that some of these modifications will persist post-pandemic, as they enable services to be more accessible for many (but not all) women. This excellent series of papers will help practitioners in Italy and elsewhere deliver high quality perinatal mental health services and provide opportunities for optimising service developments post-pandemic. The challenge will be to establish which modifications are effective, for whom and in what circumstances. This may differ somewhat by country but there will be much to learn from each other – and this series of papers is a great place to start – as we compare outcomes and improve wellbeing for women and their families, during and post pandemic, internationally.

Louise M. Howard

According to the most recent estimates, approximately 10-20% of women suffer from mental health problems during the perinatal period [2]. Indeed, perinatal mental disorders (i.e., mental health problems emerging during pregnancy and/or within the first year after the partum) are very common, with one to two women out of 1,000 requiring a psychiatric admission in the first few months after birth [3]. It has been estimated that for each woman requiring psychiatric admission following birth, at least two more women require an outpatient treatment, and 12 women receive a pharmacological treatment in primary care [4].

Unfortunately, the fact that the perinatal period is a robust risk factor for women's mental health has been neglected for a long time [5]. Moreover, the perinatal period constitutes a relevant threat for the long-term mental health for the infant, with considerable morbidity and mortality [6]. In fact, the presence of perinatal mental disorders in the mother is associated with negative outcomes in the new-born, including increased risk of premature delivery, infant mortality, and development of mental disorders (e.g., attention deficit or anxiety disorders) in childhood or adolescence [7].

The ongoing health and social crisis due to the COVID-19 pandemic is likely to produce additional stress for pregnant women, affecting their mental health [8, 9]. In fact, pregnant women may develop worries and concerns about the risk of infecting and transmitting the virus to the infant [10]. Moreover, the containment measures, such as physical distancing, quarantine and self-isolation, have reduced the access to health services, with an additional burden for perinatal health services.

During the perinatal period, an optimal psychiatric plan for women should include not only the management of the "common mental disorders", such as depressive and anxiety disorders, but also suicidal ideation, suicidal attempts, substance misuse and psychosis. The World Health Organization (WHO) [11] has recently highlighted the need to implement community-based mental health and social care services for early identification and management of maternal mental disorders. Therefore, in order to adequately manage women's perinatal mental disorders, there is the need to develop and disseminate integrated interventions, following a comprehensive global assessment of women's mental health.

In this *Annali* Monograph entitled "New perspectives in perinatal mental health models: facing challenge for Italian health services", new models for screening, care and treatment are presented. In particular, the obstacles and advantages of the implementation of the Australian model of treating perinatal anxiety and depression are discussed, and data on the Italian progresses and challenges are presented and discussed.

A specific focus is dedicated to suicidality. Suicide represents a leading cause of maternal mortality, and a multidisciplinary team, including general practitioners, gynaecologists, midwives, paediatricians and psychiatrists, is essential. Providing a long-term support to women at particular risk may reduce self-harm and suicide mortality and can improve the well-being

of the new-born, the father and of the whole family network.

The impact of the COVID-19 pandemic on perinatal mental health is also discussed in this Monograph with the adaptation of an intervention programme during emergencies. This programme includes increasing women's awareness on perinatal mental health problems and proposing screening procedures to all pregnant women, and it looks promising. The adaptation of this programme highlights the capacity of mental health services to rapidly adapt to the evolving situation of the COVID-19 pandemic.

In conclusion, I am very glad to the authors of this Monograph to raise awareness on the problem of the timely recognition and adequate treatment of perinatal mental health disorders, which is a public health priority due to its significant impact on short- and long-term women's health and child development. There is the need to further develop, disseminate and implement screening programmes, supportive interventions and good clinical practices in order to adequately treat women with perinatal mental health problems.

Andrea Fiorillo

The issues enclosed in this Monograph reflect the rigorous commitment of the researchers at the Italian National Institute of Health in the field of Perinatal Mental Health, to promote scientific knowledge, professional training program and to implement evidence-based psychological interventions in the community [12-14].

Birth is one of the critical life events. It involves a re-definition of roles, a relational renegotiation and it can be considered a stressful event, that is, potentially active in mobilizing, or determining a lack of psychological resources to manage new conditions. During pregnancy and one year after their baby is born, studies show that one in five women has mental health problems, mainly anxiety and depression [15]. These problems weaken a woman's ability to care for her baby and to build an effective emotional relationship with him/her. Besides, they can affect the attachment and mother-infant interaction, leading to potentially long-term disturbances in the infant's physical, emotional, cognitive and social development. In severe cases, perinatal depression and anxiety can lead the woman to extreme gestures. Suicide is a leading cause of death in women of childbearing age.

When we talk about perinatal mental health, we usually refer to the mother but it would be desirable to think of both parents, because, although less frequently, also the father can manifest problems, and a paternal condition of non-perfect balance can affect mother's health.

Fortunately, perinatal depression is identifiable and treatable. However, there are a series of challenges that must be faced to design interventions capable of preventing the onset of conditions of mental distress through the development of individualized paths dedicated to promoting mental health, not only of the mother-child dyad but also of the partners and the family and social context in which they are inserted.

These conditions need to be identified early. We have

many tools available, but still today, about half of the women who present discomfort in the perinatal period is not identified and do not receive appropriate treatment. It is, therefore, necessary to reflect on the services and professionals who can best intercept the difficulties of the woman, on which screening tools are the most appropriate to use during pregnancy and postpartum to intervene and finally, on the diagnostic criteria to be used. Furthermore, there is still little attention paid to the risk factors underlying these problems, as well as to the contextual conditions that can multiply the risk of discomfort [16].

In our country, there is a widespread network of Health Services that deal with perinatal mental health and it is necessary to strengthen and reorganize them from both a quantitative and qualitative point of view by enhancing the professionals' skills, whose knowledge must be constantly kept up-to-date and based on the growing scientific evidence. The work of Family Consultants, Clinical Psychology Services and Mental Health Centers must be connected to that of Social Services and integrated into a dimension of continuity, proximity and appropriateness of care [17-19].

Fabrizio Starace

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An Australian perspective on treating perinatal depression and anxiety: a brief review of efficacy and evidence-based practice in screening, psychosocial assessment and management

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Abstract

Australia is at the forefront of developing screening practices, interventions and national public health policy for perinatal women with depression and anxiety. For the last two decades Australian mental health experts and public health administrators have conducted population-wide feasibility studies on screening and incorporated these in national guidelines. This chapter outlines the wider evidence base supporting current Australian practice. Key recommendations include use of the Edinburgh Postnatal Depression Scale or the Patient Health Questionnaire-9 early in pregnancy and at 6-12 weeks postpartum, followed by psychosocial assessment. Positive depression screens need to be followed by diagnostic assessment, and clear treatment pathways must be available. Milgrom and colleagues' cognitive behavioural treatment is the only Australian program with a solid evidence base demonstrating its effectiveness for depression and associated anxiety. The face-to-face treatment has been further developed into an online program, MumMood-Booster, funded by the Federal government and available to Australian women.

Key words

- perinatal
- depression
- anxiety
- screening
- treatment

HISTORY OF SCREENING POLICY IN AUSTRALIA

Maternal mental health has increasingly gained public and scientific focus in Australia. A major catalyst was the foundation of beyondblue, an independent, not-for-profit national depression initiative funded by the Commonwealth and Victorian State governments, in 2000. Beyondblue brought together perinatal mental health experts in each State and established the National Postnatal Depression Program (NPDP: 2001-2005). This feasibility study, which aimed at implementing screening and early intervention programs for antenatal and postnatal depression, involved 40,000 women during pregnancy and 120,000 women postnatally as well as training of health professionals across 8 states over 5 years [1].

The demonstration of effective screening practices culminated in a National Action Plan recognising the perinatal mental health needs in Australia at that time [2]. Grounded on the principles of health promotion,

prevention and early intervention, the new Plan formulated recommendations around the resources and structures (both at policy and operational level) essential for implementation of depression screening, psychosocial assessment, training and workforce development for healthcare professionals, and the provision of quality pathways to care. The release of the National Action Plan led to a commitment of \$85 million by the Australian government for the establishment of the National Perinatal Depression Initiative (NPDI; 2008-2015). Extensive work, including public health initiatives, research, strategic planning, advocacy and government investment, has been undertaken under the umbrella of this Initiative.

Importantly, the NPDI supported the development of the first Australian Clinical Practice Guidelines for Depression and Related Disorders in the Perinatal Period [3]. Backed by a comprehensive systematic literature review and expert consensus, these Guidelines played a key role in guiding best practice for identifying

perinatal depression, with recommendations for universal screening and pathways to care to reduce maternal mental health morbidity. In 2017, these guidelines were updated to reflect the advances in research and innovation and to broaden the scope to include assessment of risk factors and additional perinatal mental health conditions [4].

Treatment of a range of perinatal mental health conditions has been facilitated by Australia's universal health insurance scheme, Medicare, which provides access to universal medical care and subsidized sessions for psychological and psychiatric services for all perinatal women with a depression diagnosis.

SCREENING FOR DEPRESSION AND ANXIETY - GENERAL CONSIDERATIONS

Universal screening tools

Routinely asking women about their mental health, often with the use of a screening tool, can help identify women who would not ask for help spontaneously due to various reasons, including stigma, denial and lack of knowledge [5]. Opportunistic screening for postnatal depression based on clinical judgment alone has been demonstrated to miss many depression cases [6]. Routine, universal postnatal depression screening using validated tools, on the other hand, has been shown to increase rates of diagnosis and therapy initiation [7]. This may be attributed, at least partially, to routine screening being highly accepted by women [8] and refused only by few women [7]. This evidence supports the importance of routine, universal screening for perinatal depression which has become policy in Australia [4]. Furthermore, evidence from Australian screening research suggests that even when positive screening results do not lead to a diagnosis of depression, they often indicate the presence of other mental health conditions [9].

There are multiple universal tools available for screening for perinatal depression, including generic and perinatal-specific tools (see a review [10] and a comprehensive text by Milgrom and Gemmill [11]), and several considerations should be made when selecting the appropriate tool. A brief, self-administered tool is often favourable in perinatal settings where limited time is available for screening by health professionals. Of utmost consideration is the tool's sensitivity and specificity which indicate the tool's ability to identify all true cases and non-cases. Sensitivities of postnatal depression screening instruments vary largely and are highly dependent on the cutoff values by which an "elevated" or "positive" score is determined. Specificities of the various screening tools also range widely, with lower cutoff scores associated with lower specificities. Whether a tool is available in other languages and has been validated across several ethnic populations could also be of importance if to be used in women with linguistically and culturally diverse backgrounds (for example [12]).

Two widely used validated screening tools are the Edinburgh Postnatal Depression Scale (EPDS; [13]) and the Patient Health Questionnaire-9 (PHQ-9; [14]). The EPDS is a brief, self-administered tool. An EPDS cutoff value of 13 is commonly applied and has sensitivities of ~80% and specificities of ~87% for depression, although

values vary depending on characteristics of the sample. Lower cutoffs have been used at times for population screening with sensitivities close to 100% but resulting in more false positives [15]. The PHQ-9 also has the advantage of being a brief, self-administered instrument. Studies validating the tool with a cutoff value of 10 have reported sensitivity and specificity of 75% and 91% for postnatal depression [16] and 85% and 84% for antenatal depression [17]. The PHQ-9 has been used as both a primary screening tool and as a confirmatory test for women identified as possibly depressed by the EPDS (>10) [18]. Being sensitive to changes in depression severity (including for postnatal depression), the PHQ-9 is also suitable for assessing response to therapy [18]. In addition, PHQ-9 baseline depression severity can assist clinicians in selecting the appropriate treatment [19] and in facilitating follow-up management, particularly in primary care setting [18].

As maternal suicide and infanticide are two of the most severe adverse consequences of postnatal depression [20], it is of utmost importance to recognise and evaluate thoughts of self-harm and infant harm during depression screening. Both the EPDS and the PHQ-9 can be used to identify maternal suicide as they have embedded questions related to self-harm or suicidal ideation [13, 14], however, neither asks directly about risk of harm to the infant.

An alternative method for the multi-item self-report screening tools, is the use of ultra-brief case-finding questions as a first-step approach. The PHQ-2 [21], a shortened two-item version of the PHQ-9, can be administered initially and if scored high should always be followed by administration of the PHQ-9 [16]. The PHQ-2 has a sensitivity of 84% and a specificity of 79% for the detection of postnatal depression [16]. The "Whooley questions" comprise a 2-item tool derived from the PHQ-2 with a timeframe of 4 rather than 2 weeks and scored only as yes/no responses [22, 23]. The Whooley questions have been reported to have a sensitivity of 100% and a specificity of 65-68% in identifying depression in antenatal and postnatal women [23]. Among screen positive women, a third question is used in some settings, asking women if they desire help for their symptoms and has been reported to reduce sensitivity to 39-58% and increase specificity to 91-100% [23]. The National Institute for Health and Care Excellence (NICE) guidelines recommend to initially administer the Whooley questions, and if one of these questions is answered positively it should be followed by either the EPDS or the PHQ-9 [24]. A recent study by Howard and colleagues [25] has shown that when routinely asked in early pregnancy, the Whooley questions had sensitivity of 41% and specificity of 95% and was useful as a case-finding tool as part of a general discussion about health. Further assessment was needed as positive responses suggested that women may have a mental health disorder (not necessarily depression).

Anxiety is often co-morbid with depression and can often have a major impact on functioning. Screening tools for perinatal anxiety have a more limited evidence base and therefore the Australian guidelines recommend to screen for anxiety based on clinical judgment

[4]. In the United States, the Women's Preventive Services Initiative has recently released a recommendation to screen all women above 13 years of age for anxiety, including perinatal women [26]. The Generalized Anxiety Disorder-7 (GAD-7; [27]) screening tool was found to be useful for identifying GAD during and after pregnancy [28]. An abbreviated version of the GAD-7, the GAD-2, is also available [29] and is recommended by the NICE guidelines to be administered initially and followed by GAD-7 if necessary [24]. A subset of the EPDS, items 3-5, have also been used for initial anxiety screening and require further assessment [30]. Perinatal specific anxiety tools have also generated interest due to the specific stressors associated with pregnancy and the postpartum [11].

To summarize, it is currently recommended that screening for depression in the perinatal period will be conducted by administering either the EPDS using a cutoff score of 13 or the PHQ-9 using a cutoff score of 10. Both are brief, self-administered instruments that also assess for suicidal ideation and are readily available in the public domain. In addition, both tools have been validated in several languages. The PHQ-9 is also useful when monitoring response to postnatal depression therapy is of interest. Two- or three-question screeners, such as the PHQ-2 or the Whooley questions, can be administered even more rapidly and with high sensitivity, but may not be as specific for identification of depression per se and may yield higher numbers of false positive. When a positive response to these screeners is obtained, it is recommended that these brief tools are accompanied by a more comprehensive tool such as the EPDS, PHQ-9 or a diagnostic assessment. Screening tools for perinatal anxiety require further investigation prior to recommendations for widespread use.

Settings required for screening

Screening necessitates specific settings to ensure it is conducted in an effective and a respectful manner to support high-risk women through their journey towards treatment and remission. Several considerations need to be made in regard to who should screen, and where and when screening should occur. Screening should be undertaken only by health professionals who have appropriate training and skills. In Australia, despite recommendations for universal screening having been in place for over a decade, only 69% of midwives report ever screening for postnatal depression [31]. In addition to time constraints, one of the causes of this relatively low screening rate could be due to health professionals feeling uncomfortable asking women about depression and may be concerned that some women will even react negatively [32]. Increasing health professionals' willingness to screen and their comfort with the screening tool are therefore essential components of screening training programs. Although training for screening is well integrated into routine practice and is accessible, particularly at the level of "basic knowledge", there are still areas where training has not been comprehensive. Whilst increasing identification rates is the key goal, focus should be given also to minimizing potential harms connected with screening, such as misdiagno-

sis, labelling and stigma. Therefore, training programs should be designed not only to educate health professionals on how to use the appropriate screening tools but also to support them in developing communication skills that will allow them to administer these tests in a women-centred and culturally safe manner [33].

An appropriate screening site would be one that women are likely to attend as part of their scheduled antenatal, postnatal or home visits. In addition, screening site should also offer services beyond screening, i.e. evaluation, treatment, follow-up and monitoring [7, 18]. Studies have shown that less than 50% of women with elevated screening scores who are referred for further evaluation or treatment actually follow that referral through (for example [34, 35]). Offering on-site follow-up services for diagnosis or treatment may increase the site's ability to improve outcomes [7, 18]. However, barriers to full implementation still exist even for sites that offer continuity of care. These barriers include time pressures, inadequate funding, absence of referral resources for complex cases and lack of training [36]. One way to overcome some of these barriers is by electronic screening (e-screening) such as the Australian e-screening platform iCOPE, which allows women to complete the self-report tools on a mobile device or tablet [37]. Innovations such as coupling e-screening with clinician decision support systems and production of electronic management reports are currently being trialled in Australia with a system called the Perinatal Identification, Referral and Integrated Management for Improving Depression (PIRIMID system). Postnatal depression screening in sites outside of health care facilities, perhaps even self-screening, may be necessary for 3%-15% of women in industrialized countries (higher rates in developing countries) who do not attend postpartum visits [6].

The optimal timing for screening during pregnancy and postnatally is yet to be determined. The times available for screening during pregnancy depend largely on the woman's timing of seeking antenatal care and the timing of the delivery. Whilst screening at any stage throughout pregnancy may detect prevalent depression and anxiety, screening at 34 to 36 weeks could also point to a risk of developing postnatal depression [38]. However, postpartum screening before women are discharged from the hospital post-delivery for depression as early as 24 to 48 hours postpartum has a limited ability to predict continued depressive symptoms due to high rates of false positive screens caused by 'baby blues' and the physical and emotional upheaval associated with a complex delivery or unexpected outcome. Early post hospital screening, at 5 days postpartum, had lower specificity and sensitivity in comparison with screening at 6 weeks after delivery [39]. When evaluated at 6, 8 and 12 weeks postpartum, the effectiveness of screening in identifying women at increased risk for prolonged postnatal depression was comparable [40]. Therefore, screening at these times which are part of the health care visits schedule (e.g. routine 6-8-week postpartum visit) may be done effectively by taking advantage of current health care delivery patterns. In terms of re-screening, a study by Yawn and colleagues

has demonstrated that screening at 6 and 12 months postpartum may identify additional women at risk that were screened negative at 4 to 12 weeks postpartum [41]. With respect to the optimal timing of anxiety screening in the perinatal period, due to lack of studies no evidence-based recommendations can be made. However, from a pragmatic point of view, it seems most efficient for anxiety screening and depression screening to coincide.

To summarize, it is currently recommended that screening will be conducted by health professionals who have received training in woman-centred communication skills and culturally safe care and are comfortable with screening. Screening should be completed at a place that is convenient for women and that offers follow-up services, especially provision or referral to evidence-based treatments. In terms of timing, it is currently recommended that the first antenatal screening will be completed as early as practical in pregnancy and will be repeated at least once later in pregnancy. Evidence supports first postnatal screening at 6 to 12 weeks postpartum and re-screening at 6 to 12 months postpartum. No evidence currently exists in regard to the optimal timing of anxiety screening, but if such screening becomes policy, concurrent screening for depression and anxiety seems most practical until evidence emerges.

Interpretation of screening results and referral for further assessment

When an EPDS score between 10 and 12 is obtained, recommendations often suggest that the EPDS should be repeated within 2-4 weeks [4]. A similar re-screening is suggested for PHQ-9 scores between 5 and 9 [42]. Elevated screening scores (EPDS ≥ 13 ; PHQ-9 > 10) should be followed by a diagnostic assessment and a suitable follow-up. A positive score on the suicidal ideation item (EPDS question 10; PHQ-9 question 9) or a very high total score may indicate the woman is at risk of harming herself and/or her child, and therefore must be immediately followed by risk assessment. If suicidal ideation is indicated in the risk assessment, an urgent action should be taken in accordance with local protocol/policy [4].

In a small percentage of women, high depression and anxiety screening scores could be a manifestation of a general medical condition, such as hypothyroidism, hyperthyroidism [43] and anaemia [44] or other psychosocial conditions, including baby blues, problems with managing marital relationship and poor social support amongst others [45]. Thus, in some women with positive depression or anxiety screening diagnostic assessment should be accompanied by a thorough medical and psychosocial evaluation.

There is an ongoing debate in regard to what is considered an adequate diagnostic assessment for a positive screening score. Whilst some health professionals argue that positive screening results require a standardized diagnostic interview by a trained mental health professional [46], this can prove impractical given the need to evaluate 15-25% of pregnant women and shortage of mental health professionals [47]. Limited but

growing evidence supports an alternative approach by which a diagnostic assessment can be carried out in primary settings by a clinician trained in the diagnosis and management of depression [7, 48, 49]. The assessment must include an evaluation of symptoms severity and duration and whether the symptoms impact the woman's ability to function in her usual roles. Evaluation of other signs of mental health disorders such as bipolar disorders, psychotic disorders (including postpartum psychosis), anxiety disorders and substance use disorders must also be considered [20]. Women with unusual presentations, history of serious mental health problems and depression resistant to therapies available in the primary setting deserve a referral to a mental health professional [7, 18].

When a diagnosis such as postnatal depression is made, a crucial step in seeking help would be engaging the woman and, if possible, members of her support network in a discussion concerning her depression and help seeking [50]. Patient engagement is also important for initiation and adherence to therapy and participation in follow-up and monitoring visits or phone calls [7, 51].

In summary, it is currently recommended that for a woman with an EPDS score between 10 to 12 or with a PHQ-9 score between 5 to 9, screening should be repeated, for instance within 2-4 weeks. Women with an EPDS score of 13 or more or with a PHQ-9 score of 10 or more should be referred to a diagnostic assessment for depression. Women who are scored positive on EPDS Question 10 or on the PHQ-9 Question 9 should undergo immediate risk assessment, and if there is any disclosure of suicidal ideation, an urgent action should be taken in accordance with local protocol/policy.

ASSESSING BEYOND DEPRESSION - PSYCHOSOCIAL ASSESSMENT

Identifying psychosocial risk factors

It is now recognised that perinatal mental health is multifaceted and is much broader than the simple diagnosis of postnatal or antenatal depression. Whilst major depression is the most common perinatal mental health condition, for some women increased psychological vulnerability during the perinatal period may give rise to new onset psychiatric episodes or relapse of pre-existing psychiatric episodes (often due to discontinuation of medication in pregnancy) other than major depression, for example, puerperal psychoses [52] and bipolar disorder [53, 54]. Furthermore, in women presenting depressive symptoms, symptoms can be an indicator of distress triggered by complex and serious psychosocial co-morbidities and adverse circumstances, such as interpersonal violence, substance use and a history of adverse childhood experiences. When major depression is diagnosed, addressing these co-morbidities is essential for the depression to respond well to the usual treatment modalities [55]. The implications of such complex cases going undetected and untreated can be devastating. Psychosocial illness (including substance use and interpersonal violence) has been found to be one of the leading causes of maternal deaths in higher income countries [56, 57]. Furthermore, admission for a severe

psychiatric episode in the first postnatal year leads to 70-fold increase in the risk of suicide compared to at other times in her life [58]. These complex cases may also have deleterious impact on the infant [59]. Hence, identifying the presence of psychosocial factors which may increase a woman's vulnerability to experience perinatal mental health morbidity and thereby providing them with the most suitable care, is crucial.

Several key risk factors for poor perinatal mental health have been identified with the most consistently reported being a past history of a mental health condition, including major depression and anxiety disorder [33, 60-61]. Other major, consistently reported risk factors for postnatal depression include antenatal depression symptoms, antenatal anxiety, major stressful life events, lack of practical/emotional support and poor partner support [61]. Considerable evidence supports the association with additional characteristics such as poor marital relationship including interpersonal violence, a history of childhood trauma, isolation (physical, mental, cultural), substance use and long-standing personality vulnerabilities [33, 62-65].

Evaluation of current and longstanding psychological, social, and cultural risk factors is the essence of psychosocial assessment programs [66]. Research shows that enquiring about women's emotional health is an essential step towards seeking formal mental health care in the perinatal period [67]. The Australian guidelines note the use of universal psychosocial assessment as a good practice point and recommends assessing for psychosocial factors as early as practical in pregnancy and at 6-12 weeks after birth. In addition, the Australian guidelines note enquiring about the woman's emotional wellbeing at every antenatal or postnatal visit as a good practice point [4]. Similarly, the NICE guidelines advocate a broad psychosocial assessment approach [24]. The value of psychosocial assessment lies in the opportunity it provides for raising awareness and educating women and families as well as 'starting the conversation' around psychosocial risk factors. In addition, this provides an opportunity to locate supports as protective factors to assist in the prevention of mental health problems. Research has shown that asking about the woman's past and/or current mental health led to higher rates of referrals [68].

Psychosocial assessment methods

Different approaches can be adopted to effectively undertake psychosocial assessment in primary settings. These approaches range from the use of psychosocial assessment tools, either self-report or clinician administered, to a general unstructured enquiry as part of holistic care. Structured questionnaires have the advantage of providing a comprehensive, brief overview of the woman's circumstances by covering key risk domains, thereby allowing to start the conversation to further explore particular domains as needed. Such tools could be especially useful for health professionals who are not experienced in undertaking a detailed psychosocial assessment as part of the broader interview. The Australian guidelines note ensuring health professionals receiving training in the importance of psychosocial as-

essment and use of a psychosocial assessment tool as a good practice point [4]. Several structured psychosocial assessment tools are available and include the Antenatal Psychosocial Health Assessment (ALPHA), Antenatal Risk Questionnaire (ANRQ), Predictive Index of PND, and the Antenatal Psychosocial Questionnaire [67]. A validated, user-friendly and acceptable psychosocial assessment tool or structured interview that is suited to the local primary care setting can facilitate a comprehensive assessment.

Interpretation of psychosocial assessment results and referral

Psychosocial risk factors identified through a structured tool or as part of a broader clinical interview need to be further explored and documented. It is recommended to undertake psychosocial assessment in conjunction with depression screening [4] and integrate them in care programs which also entail further mental health evaluation and management [69]. Interpretation of the results of the psychosocial assessment is determined by local decision-making rules in the context of the depression screening results [70]. Decision-making rules could be applied in the form of an algorithm which assists clinicians to determine through a multidisciplinary approach whether women have a mental health condition, including current possible depression. Alternatively, the use of a clinician decision support system such as the one currently being trialled in Australia (PIRIMID) allows health professionals to use clinical judgement in interpreting which risk factors should be addressed in a management plan and integrate this with other clinical information. This allows identifying women at high psychosocial risk and devising an appropriate care plan for them [71].

TREATMENT

Perinatal mental health care is a 3-stage process entailing screening and psychosocial assessment, referral, and treatment. An integrated approach that seamlessly links screening and psychosocial assessment results to a defined referral process and treatment can optimize treatment accessibility, completion, and response. This in turn will result in a more clinically and cost-effective means for managing perinatal depression and anxiety [72].

The next step following diagnosis of antenatal or postnatal depression would be selecting the appropriate treatment approach that is likely to result in remission of depressive symptoms and is available in the immediate region. Systematic reviews have confirmed the effectiveness of a range of treatment approaches for perinatal depression, including pharmacotherapy, cognitive behavioural therapy (CBT), counselling and interpersonal therapy (IPT) [73-76]. In comparison, treatment studies for perinatal anxiety have received relatively less attention. It is expected that treatments that are effective for anxiety at other life stages would also be effective for anxiety during the perinatal period, and there is evidence for CBT for perinatal anxiety [77], which is the best practice treatment for anxiety disorders in the general population. There is also evidence emerging

for e-Health interventions [78], and mindfulness-based interventions [79].

Pharmacotherapy

Some trials for postnatal depression have reported positive results whereas others have been more ambiguous [80, 81]. Nevertheless, it seems likely that the efficacy of antidepressant medications in depressed postnatal women would be similar to the efficacy of antidepressant medications observed in the general population, including non-postnatal women [82]. In addition, when comparing antidepressants with psychological treatment, there may be different relative benefits; for example, a more rapid effect of medication versus better relapse prevention for psychological treatment [83]. A meta-analysis of the overall evidence emerging from randomized controlled trials (RCTs) in postnatally depressed women suggests that it is not clear whether antidepressants are superior to psychotherapy, or whether some antidepressants are more effective or better tolerated than others [76].

During pregnancy and breastfeeding, before starting antidepressant treatment, the potential harmful effects on the developing fetus and on the infant need to be considered alongside the potential harm if the woman remains untreated or ceased medication [84]. The Australian guidelines outline specific considerations in the use and monitoring of the effects of pharmacological treatments drawing upon the NICE clinical guidelines. This includes consideration of the woman's past response to antidepressant treatment, obstetric history (e.g. other risk factors for miscarriage or preterm birth if pregnant) and any factors that may increase risk of adverse effects (e.g. when breastfeeding, considering the infant's health and gestational age at birth) before choosing a particular antidepressant [4].

Whilst the use of selective serotonin reuptake inhibitors (SSRIs) is often used in primary care as a first-line treatment for moderate to severe depression, this needs to be balanced with women's preferences and the known efficacy of psychological treatments for this group. For example, we know that the majority preference among perinatal women is to avoid such pharmacological treatments where possible [5].

Psychological approaches to treatment

Psychological treatment is a viable first-line of treatment for mild to moderately severe depression and an alternative for women who are pregnant or breastfeeding and therefore prefer not to take antidepressants. Previous evidence supports the efficacy of various psychological treatment approaches for maternal perinatal depression [73-75]. Although CBT and IPT are the most beneficial, IPT has a somewhat narrower evidence base in perinatal populations than CBT. The Australian guidelines note treatment with CBT and IPT for women with mild to moderate depression in the perinatal period as an evidence-based recommendation [4].

CBT – In Australia, Milgrom and colleagues have developed well-evaluated face-to-face and online CBT programs for perinatal depression. We have developed a 12-week group CBT program, Getting Ahead of Post-

natal Depression, for postnatal depression [85] drawing upon the CBT content embodied in Lewinsohn's well-validated 'coping with depression course' [86] to accommodate unique needs of depressed mothers with new infants. Evaluated in two RCTs, the program was found to significantly ameliorate depressed mood and was superior to routine care [87] and effective to the same extent as pharmacotherapy with sertraline [88]. A modification of the Getting Ahead of Postnatal Depression program developed for antenatal women, Beating the Blues Before Birth, was also evaluated in a feasibility trial and an RCT and proved highly effective in reducing both depression and associated anxiety in pregnant women diagnosed with depression (80% with major depressive disorder) [89]. An antenatal self-help program also developed by us, Towards Parenthood, aimed at preventing early parenting and coping difficulties, and was found to be effective in an RCT [90]. Another postnatal depression treatment program (Overcoming Depression Program) developed for delivery by nurses working with general practitioners was trialled and showed promising results in reducing depressive symptoms [49].

Internet-based interventions have been increasingly used to address maternal depression and a range of psychological problems experienced by perinatal women [91]. The value of internet-based delivery of treatment programs lies in its potential to overcome major barriers to treatment uptake in perinatal populations, such as stigma and lack of reach of traditional services [5]. Being anonymous, accessible, affordable and convenient, internet-based depression programs have the potential to reach many women who otherwise would not access treatment.

Milgrom and colleagues have rigorously developed and evaluated an online CBT intervention for treating postnatal depression (MumMoodBooster; [92]). This innovative program was adapted from the face-to-face Getting Ahead of Postnatal Depression treatment program and the subject of extensive usability and feasibility trials. It was developed to mimic face-to-face treatment and has features which allow individual tailoring of the targets of intervention, using a range of features including host videos and feedback of progress. The effectiveness of this intervention was evaluated in an RCT comparing the online CBT treatment (n=21) to treatment as usual (n=22). At 3 months post-enrolment, a four-fold increase in remission was observed, as 79% of women in the intervention group no longer met the diagnostic criteria for depression compared to 18% of women in the treatment as usual group. Improvement in measures of depression, anxiety and stress was also more evident in the intervention group [93]. In another RCT the intervention was found to be at least as effective as face-to-face CBT at 6 months post-treatment (in preparation). In light of previous evidence indicating that guided support increases the effect size of self-guided internet interventions in the general population with depression [94], coaching support was offered to women in conjunction with MumMoodBooster to increase severely depressed women's adherence to treatment. An antenatal version of this

program, Mum2BMoodBooster, has also been developed and evaluated in a feasibility trial yielding promising results in regard to its effectiveness in reducing depression and anxiety symptoms in pregnant women (in preparation). MumMoodBooster, both the postnatal and the antenatal versions, are funded by the Federal government and available to all Australians through MumSpace. MumSpace is a digital platform developed by the Perinatal Depression e-Consortium with the aim to provide a stepped-care approach for prevention and early, self-help intervention to ameliorate perinatal depression and thereby reduce the burden on more traditional acute downstream services.

IPT – An Australian RCT evaluating the effectiveness of group IPT for postnatal depression has shown that group IPT yielded a greater improvement in depressive symptoms compared to treatment as usual at 3 months post-therapy [95]. In another study following these women up to 12 months post-therapy it has been shown that women in the IPT group were less likely to develop persistent depressive symptoms [96].

Combination therapy

Studies exploring the efficacy of combined psychological and pharmacological therapies for postnatal depression have reported little or no benefit. For example, in a study by Misri and colleagues [97] the effects of paroxetine both alone and combined with CBT were found to be comparable. Likewise, combination of sertraline with psychological therapy did not attract additional benefits in our Australian study or that of Bloch and colleagues [88, 98]. However, some women report that the adjunctive use of psychological treatments and pharmacotherapy can be helpful; for example, rapid relief of symptoms followed by greater availability to psychological treatment, usually once medications have become effective [4].

Mother-infant interventions

Symptoms of postnatal depression, including sadness, flatness and loss of interest, as well as symptoms of comorbid anxiety, can make it difficult for some depressed women to engage behaviourally and emotionally with their infants [99, 100]. Mother-infant interactions are complex and involve reciprocal micro behavioural exchanges between a sensitive and attuned mother and a developing infant that are vital for optimal infant development [101]. Depressed mothers are less likely to be responsive and sensitive to infant's cues, less engaged in affectionate physical contact, make less eye contact with their infants, and may be intrusive in their interactions [99]. Such dysfunctional mother-infant interactions have been shown to mediate the impact of postnatal depression on child development [99].

A number of studies have shown that effectively

treating postnatal depression does not necessarily result in improved mother-infant relationships (for example [87]) and there is therefore a need for complemented interventions designed to target the mother-baby relationship (see a review [102]). In Australia, Milgrom and colleagues developed a brief, targeted mother-infant interaction intervention called 'Happiness Understanding Giving and Sharing' (HUGS [85, 103, 104]), which complements CBT treatment for maternal postnatal depression. A pilot study of HUGS showed rapid reductions in stress in the mother-infant dyad, which was a weekly rate of reduction that was three times larger than during earlier treatment for postnatal depression [103]. This was followed by an RCT comparing HUGS to a control playgroup following postnatal depression treatment, which showed significant improvements in both observed and parent-reported mother-infant interactions.

FUTURE DIRECTIONS

Over 300,000 women give birth in Australia each year and up to 20% experience clinical depression, often with severe anxiety, either in pregnancy or in the first postnatal year. Despite the substantial progress in screening and treatment implementation, low treatment uptake rates remain concerning. Future efforts require strategies to bridge the gap between cases identified by screening and the number of women receiving treatment resulting in remission from their depressive episode [11]. Furthermore, the harm through the continued non-identification and non-treatment of the majority of cases of perinatal depression underlines the continuing importance of increasing identification rates and providing adequate treatment for women experiencing perinatal depression and anxiety. From a societal and economic perspective, perinatal depression and anxiety in Australia incur an enormous burden mostly borne by children, which is estimated at \$7.3 billion [105]. Taken together, identifying and treating perinatal depression and anxiety is crucial both at the individual and the societal levels. However, although screening for perinatal depression is policy in Australia, further efforts need to be made to implement screening into practice with available integrated treatments. Moreover, further RCTs are needed to form a strong evidence base that will guide every aspect of detection and management of perinatal depression and anxiety each separately as well as part of an integrated process.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Feasibility and effectiveness of the Australian perinatal mental health approach in the Italian health services: progress and challenges

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Abstract

The perinatal depression is one of the leading pathologies in the world causing disabilities and represents an important public health problem. Since 2003, the Center for Behavioral Sciences and Mental Health (Istituto Superiore di Sanità - ISS) has promoted studies and research on the mental health of women, children, partners and family in the perinatal period, leading to the realization of a structured program adopted in many Italian services. In this article, we describe the feasibility and effectiveness of the perinatal mental health approach in Italian health services and discuss the progress and new challenges.

Key words

- perinatal mental health
- screening
- treatment
- depression
- anxiety

INTRODUCTION

For some years now, anxiety and postpartum depression have been the subject of growing attention and interest from scientific, academic and healthcare professionals. The World Health Organization (WHO) estimates that 10% of pregnant women and 13% of women who have just given birth suffer from a mental disorder, mainly depression [1].

A recent systematic review [2] that considered 58 studies involving a total of 37,294 healthy women, reported an estimate incidence for postnatal depression of 12% and a prevalence of 17% with higher prevalence in low- and middle income countries than in high income countries [3] also emphasizing that post partum depressive and anxiety symptoms frequently begin during or before pregnancy [4, 5] but women are less likely to receive treatment during pregnancy than postnatally [6].

Prevalence studies conducted in Italy indicate that depression affects 1.6% to 26.6% of women during the perinatal period [7-15]. However, perinatal depression is underestimated due to women denial or isolation and this problem could be underdiagnosed [16, 17].

Furthermore, depression is one of the leading pathologies in the world causing severe dysfunction at work, at school and in the family and represents an important public health problem, with a high subjective or objective burden, direct and indirect costs due to the impairment of personal, social and occupational functioning [1]. In addition, it should be considered the long-term consequences that maternal postpartum depression has on mental health and development of children.

Since 2003, a group of researchers from the Center for Behavioral Sciences and Mental Health (Istituto Superiore di Sanità – ISS) has promoted studies and

research on the mental health of women, children, partners and family in the perinatal period, leading to the realization of a structured program adopted in many Italian services.

The program named “Prevention and early intervention for the risk of postpartum depression”, funded by the National Center for Disease Prevention and Control (CCM) of the Ministry of Health, started in March 2012 and concluded in March 2015, has proved acceptable and sustainable to intercept parents (both mothers and fathers) who need help for an early intervention to prevent any damage that the chronic disease could cause to woman, child, mother-baby relationship, as well as the family climate in general.

STRUCTURED PROGRAM FOR PERINATAL ANXIETY AND DEPRESSION MANAGEMENT

Specific training of the personnel involved (obstetrician, nurse, psychologist, psychiatrist, gynecologist, pediatrician of free choice, general practitioner) is the key point of the program. The training should develop not only professional skills but also capacities to work in a team and to establish a familiar, empathic, welcoming, involving and absolutely non-stigmatizing climate. This will facilitate women to recognize their difficulties and to accept to be helped.

The *empowerment of knowledge* on perinatal mental health is the first step of the program during which obstetricians and gynecologists of the Family Counseling Service and Hospital Departments inform pregnant women and their partners about the importance of psychological well-being, mental health problems that can occur during pregnancy, after childbirth, and the impact on the health of the mother, of the baby, of the couple. Usually, treatments offered by the Organizations are also presented. An information notice is distributed with the telephone numbers of the professionals and units involved and women are asked to fill in a form containing the privacy policy, their personal data and the expected date of delivery. Finally, the possibility of participating in an early identification (screening) of the risk for anxiety-depression during the perinatal period is proposed.

The *screening step*, performed by trained maternal and child professionals, can take place both before and after the birth of the baby. The screening tools used are the Edinburgh Postnatal Depression Scale (EPDS) [18, 19] for assessing the risk of depression and the Generalized Anxiety Disorder Scale (GAD-7) [20] for assessing anxiety. It was also used the psycho-social and clinical evaluation form prepared and validated by the ISS [21, 12] which collects information on pregnancy and childbirth, experiences of depression or other psychiatric problems in life, any stressful events in the past 12 months and perceived family and social support. If the woman scores ≥ 12 on the EPDS questionnaire or ≥ 8 on the GAD-7 test, she is invited to undergo a clinical assessment performed by psychologists or psychiatrists of the Organizations. Particular attention is paid to assessing the risk of suicide. If the woman scores ≥ 1 on question no. 10 of the EPDS (“The thought of harming myself has crossed my mind”), it is important to under-

stand, during the following interview, if she is in danger of harming herself or the child and to evaluate the level and immediacy of the realization of suicidal intentions.

After screening, a *clinical assessment step* is performed, in the ISS study the following assessment tools were used: the Beck Depression Inventory (BDI-II) for the evaluation of the severity of the depressive symptoms [22] and the State-Trait Anxiety Inventory (STAI), for the assessment of state anxiety [23].

On the same day of or soon after (1 to 3 day) the clinical assessment, women receive feedback from the same Professional who performed it. If a risk for depression or anxiety is confirmed, the woman is invited to receive support and a psychological intervention is offered (*treatment step*). Should the professional deem it appropriate, the psychological intervention is offered also to women who have tested negative to clinical assessment but showed some borderline scores. Additionally, providing the clinical assessment and the psychological intervention in the same clinics or hospitals where the initial assessment was done has proved preferable, avoiding relocation or referral to other mental health services [24, 12].

The *treatment step* is a psychological intervention based on a bio-psycho-social approach elaborated by Prof. Jeanette Milgrom and colleagues at the Parent-Infant Research Institute (PIRI®) [25]. The applicability and effectiveness of the treatment program in the Italian context was analysed in a 2015 study promoted by the ISS [26]. This study showed that the clinical improvement of women mainly modified the presence and severity of depressive symptoms, state anxiety and mental health (as detected by SF-36); in particular, the EPDS and SF-36 Mental Component Summary (MCS) scores [27], the results showed that over 70% of the women undergoing treatment had a significant improvement in depressive symptoms and mental health in general [26].

The treatment includes a series of 10 meetings, which can be divided into individual or group sessions (with six to eight participants). The group modality, in addition to containing the costs of the treatment, allows comparison between peers, learning by modelling and the reduction of the stigma associated with depression. The treatment includes both practical and behavioural interventions, such as daily organization, the introduction of pleasant activities, relaxation and assertiveness techniques, and deeper cognitive interventions, such as the restructuring of dysfunctional thoughts related to depression and the questioning of false myths about motherhood. All the techniques are placed in the daily reality of the woman to lead her to feel more and more autonomous and competent in the management of the child. There is also a module on the couple, to encourage communication and sharing between partners, and another on mother/child interaction, to help mothers to respond correctly to the needs of their children [28].

The program ends with the *follow-up* and with the re-administration of the same tools used in the screening phase. Women who still score at high risk of depression (equal to or higher than the cut-offs) are offered to be followed up by the territorial psychiatric services, local

family counselling centers or to be reviewed with periodic home visits, depending on the local organization of the Public Health Services.

PROGRAM IMPLEMENTATION

This program, originally adopted by a few public services (consultants and hospitals) participating in the ISS study [12], has been implemented to other Italian public services, albeit with some adaptations. The implementation has required a review of the existing practices for woman mental health management and allows us to reflect on the main critical issues and strengths that the program has shown over time.

The program goes from pregnancy, birth, all the way through, to the first years of the child's life. During the different steps of the program, all the Professionals involved work in an interdisciplinary and close way. The interdisciplinary training courses and the discussion on the cases made it possible to network the skills of professionals and indirectly allowed the Services to deliver a better service.

The ISS provided training to the relevant professionals (i.e. those who come into contact with the mother and child in the perinatal period) at their local hospital or ASL. The training courses, spread over two/three days, were divided into two modules [29, 30].

Over the years, many Services have improved the material the ISS distributed during the knowledge empowerment step, providing, for example, specific language material for foreign women or creating downloadable information material via smartphone/tablet applications (in the Lombardy region) or producing informative videos to be shown in the waiting rooms of family clinics and birth centers (in the Veneto region). Dedicated help lines or walk-in clinics are also increasingly widespread. These services are often set up by local private associations with the support of the territory (e.g. UO Novara and Aulss 6 Euganea of the Brescia Observatory), showing that the collaboration between public and private is a precious resource of integration between the various Professionals and the Services involved in the perinatal field.

Additionally, screening and clinical assessment tools used in the first phase of the method were diversified across the Services. In the screening step, some Services (the North and South Districts of Aulss2 Marca Trevigiana, ASST Bergamo Ovest, the Health District of Campobasso Molise, and the Centers connected to the Perinatal Clinical Psychology Observatory coordinated by the University of Brescia [31]) added, the Positive Scale [32] and the Patient Health Questionnaire (PHQ-9) [33] to the screening tools to have an insight on how much the woman looks with confidence to the future and to monitor the severity of depression.

In the clinical assessment step have also been used the General Health Questionnaire (GHQ-12) to investigate anxious symptoms [34], the MINI PLUS (Mini International Neuropsychiatry Interview) [35] to estimate major depressive episode; the SF-36 questionnaire [36], which assesses the state of physical and psychological health; the Psychological Well-Being Scale (PWB) [37], which investigates aspects related to

psychological well-being such as self-esteem and self-efficacy; the QUIT [38], an Italian questionnaire which looks at the temperament of the child and the WHO-QOL (World Health Organization Quality of Life) [39] for quality of life assessment.

Many Services (for example the North and South Districts of Aulss2 Marca Trevigiana) have established, in the routine of the Service, the home puerperal visit by midwives for women who have given birth. This turned out to be a crucial tool because it allowed not only to intercept the woman's discomfort but also to know the family context in which the woman lives and, therefore, to identify any signs of discomfort early or on the contrary strengthen resources and protective factors.

Over the years, the Services have tried to find new ways to identify women with postnatal depression or at increased risk of. Some services, for instance, have provided local vaccination centers (for example ASST Bergamo Ovest), regularly attended by mothers for their infants' vaccinations, with informative material to intercept women at risk. Furthermore, the role played by the General Practitioner and the Pediatrician of free choice seems to be increasingly fundamental, being at times the only health professionals with whom the woman and her family have continuous contact before and after childbirth. Some Services (eg Aulss 6 Euganea) in collaboration with some pediatricians of free choice of the territory, are running a study to evaluate the possibility to administer the EPDS, on the occasion of the child's first health assessment, to identify women at risk of perinatal depression and anxiety.

In some Services (eg ASST Bergamo Ovest), activities in the perinatal area have been enriched with a series of initiatives mainly for prevention of perinatal mental health disorders. Several meetings addressed to new or future mothers have taken place. The meeting "*Mom ... what anxiety!*", for instance, discussed the management of anxiety in pregnancy and provided practical relaxation techniques. The meeting "*Daddy Archipelago*", instead, was dedicated to future fathers in order to offer them a space for discussion and sharing on issues and experiences related to the new parenting role. The meeting "*Breastfeeding Area*" offered mothers the opportunity to share their experience of breastfeeding and the possibility for operators to monitor the management of the newborn by the mother. The strengthening of these preventive services proved to be a protective factor and contributed, in an empirical way, to reduce the onset of perinatal depression and anxiety [40].

One of the most critical aspects highlighted, especially in some areas of southern Italy (for example the Health District of Campobasso Molise), is the difficulty in recruiting women, due in part to the context in which the contact takes place (hospital, often distant or difficult to reach once the woman has given birth and returned home) and partly stemming from the fear of social stigma for everything related to mental health. The belief that maternity problems can resolve themselves by relying on family support rather than that of a professional specialist still seems deeply rooted.

Overall, the proposed program was found to be very popular with women, with high percentages of adher-

ence to screening and treatment and very low drop-outs, good results in terms of efficacy and also of sustainability, considering that the treatment is short and especially if carried out in groups, inexpensive [12, 27, 41, 42]. This program is also proposed as a tool for constant monitoring of perinatal risk factors and early screening, also tested in emergencies with remote intervention modalities [43], capable to offer the woman appropriate, timely and effective treatment.

STATE OF THE ART

In 2018, an agreement was signed between the Government, the Regions and the Autonomous Provinces of Trento and Bolzano for the presentation, by the regions, of “*Projects relating to the diagnosis, treatment and assistance of postpartum depressive syndrome*” [44], which led to the financing of 16 projects from as many Italian regions. The objective of the project outlines the phases of the structured program described above: awareness-raising and information on psychic distress and the advisability of early intervention; early identification of women at risk through standardized screening and assessment tools; psychological support actions to reduce the incidence and severity of mental disorders; post-evaluation by administering the same screening and evaluation tools used in the initial phase to evaluate the effectiveness of the intervention implemented. Each region has adapted the program to the needs and requirements of its region, enhancing local realities of excellence or proposing substantial improvements in the network of services.

However, in general, there is great variability in both the tools used for screening: EPDS, Whooley questions, State-Trait Anxiety Inventory, Psychological Well Being Scale, General Health Questionnaire-12 item, Schedule of recent experiences; and the tools used for evaluating women: Post-Partum Depression Screening Scale, Parenting Stress Index Questionnaire, Minnesota Multiphasic Personality Inventory, Care Index, Clinical Outcomes in Routine Evaluation-Outcome Measure, Clinical Global Impression, Brief Psychiatric Rating Scale, Global Assessment of Functioning, Big-5 Questionnaire, Experience in Close Relationship, Connor-Davidson Resilience Scale, Brief-Cope Scale, Beck Anxiety Inventory, Patient Health Questionnaire, Mini Mental State Examination, Multidimensional Scale of Perceived Social Support [44].

To this variability is added diversity in the time of proposal of these tools: for example, depending on the region, screening tests can be proposed at the begin-

ning of pregnancy (Sicily and Tuscany), during the third trimester of pregnancy (Umbria), 30 days before childbirth (Puglia), after childbirth (Abruzzo), before hospital discharge (Basilicata), in the 6th and 12th week after childbirth (Calabria), 3-6 9-12 months during the preliminary anamnestic interview of the child (Veneto).

As for the treatments, the same Ministry notice [45] proposes differentiated treatments based on the severity of the risk, to be carried out according to a well-defined periodicity for each treatment. The interventions provided for women at moderate or high risk are individual psychological meetings, couples, interventions to improve parental function, psychiatric counselling, home visits, counselling for breastfeeding and neonatal care, infant massage and listening space. Great variability is also observed about these activities and, in general, the application in different contexts seems to depend more on the expertise of the professional present at the time in the clinical center, than on evidence-based criteria.

Finally, to our knowledge, there is a lack of studies on the results obtained with women, of evaluating the impact and effectiveness of the Projects in the various regional realities.

FINAL CONSIDERATIONS

The experiences described are testimony to the richness and variety of actions taken in the field of perinatal mental health. However, there is a need for networking between health services to coordinate interventions, share good practices and implement further efficacy evaluation studies in practice [46]. Furthermore, it would be desirable to update evidence-based guidelines adapted to the Italian situation, to have information developed systematically and to provide uniformity of diagnosis and treatment and produce appropriate and homogeneous care behaviours.

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Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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Completed suicide during pregnancy and postpartum

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Abstract

Both pregnancy and the postpartum are typical periods for the onset or relapse of psychiatric symptoms and disorders, with depression and anxiety being the most common. The prevalence of suicide spectrum behaviour is significantly higher among women with a diagnosis of depressive or bipolar disorder. Suicide during pregnancy and postpartum is a multifactorial phenomenon and a history of psychiatric illness is only one of the possible risk factors involved in suicide spectrum behaviour. The present paper highlights the importance of a complete screening for both depression and suicide risk during peripartum.

Key words

- suicide
- pregnancy
- postpartum
- peripartum

INTRODUCTION

Pregnancy and the postpartum are generally characterized by positive feelings and expectations but they may also disguise maternal stress and difficulties. Suicide is a major public health issue, with more than 800,000 people dying annually, and over recent years a growing number of reports have also identified pregnancy and postpartum as critical periods for suicide risk. Failure to complete pregnancy, the unavailability of elective termination methods and psychiatric disorders not adequately treated may actually lead to suicide during pregnancy. Unwanted pregnancies are, no doubt, a major risk factor for suicide and this is particularly true for female adolescents, whose discovery of a pregnancy may lead them to commit suicide [1]. The literature points to the early recognition of “baby blues” as opposed to peripartum depression [2, 3]. Furthermore, the postpartum period is often associated with the onset of mood and psychotic disorders that can cause post-traumatic stress, with lasting consequences for both mother and child. Postpartum psychosis is associated with an increased risk of both suicide and infanticide: up to 30% of mothers who commit filicide also commit suicide [4].

Gelaye *et al.* [5], in a review of 57 studies, found that suicidal ideation but not completed suicide was more frequent among pregnant woman compared to the general population, suggesting that pregnancy was a protective factor for suicide. However, Lysell *et al.* [6] found a weak association between pregnancy and suicide reduction, suggesting that previous studies may overestimate the protective effects of this life period in women.

Both pregnancy and the postpartum are typical periods for the onset or relapse of psychiatric symptoms

and disorders [7], with depression and anxiety being the most common [8]. Depressive symptoms occurring during pregnancy often persist postpartum, suggesting a strong relation between antenatal depressive symptoms and postpartum depression [9]. Furthermore, approximately half of postpartum depression cases have onset during pregnancy [10].

Data regarding the incidence of peripartum depression vary in relation to the assessment method used, the timing of the assessment and the population in epidemiological studies. In general, peripartum depression is present in 7-13% of pregnant women and in 7-15% of women 1 year postpartum [11, 12].

Due to the profound physiological changes during pregnancy and childbirth and the perturbations in mood, appetite, energy and sleep associated with childbirth and infant care, it has been proposed that postpartum depression differs from depression that occurs at other periods of life [13]. The American Psychiatric Association proposed the term “peripartum onset depression” to describe major depressive episodes developing during pregnancy and the postpartum period [14].

Peripartum depression is an important public health reality that affects not only the mother but also the infant and the entire family system, worsening the couple's relationship and parental care of the infant [5, 15]. The clinical presentation of peripartum depression is characterized by low mood, sadness, irritability, impaired concentration, feelings of guilt about childcare and feeling overwhelmed. However, even non-depressed postpartum women regularly experience many symptoms that commonly reflect depression in non-postpartum women, such as fatigue, appetite disturbances and sleep disturbances [16, 17].

Peripartum mood worsening and anxiety can progress rapidly and become an imminent risk to the patient and, in rare cases, the infant. Poor maternal-fetal attachment and adverse neonatal outcomes, including low birth weight, preterm birth, small for gestational age and early childhood developmental delays, are some of the most frequent aspects of peripartum depression [18] (*Figure 1*).

Peripartum depression is a multifactorial phenomenon and several psychological features are involved in its genesis, including a previous history of depression and anxiety, a negative attitude toward the recent pregnancy, stressful life events, a history of sexual abuse, reluctance to accept the baby and low self-esteem [19]. While the role of obstetric risk factors is still controversial, several studies have demonstrated that the number of deliveries, a high-risk pregnancy, postpartum complications and a mismatch between maternal expectations and pregnancy events are associated with an increased rate of depression, whereas breastfeeding is associated with a reduction in the rate of postpartum depression [20]. Glucose metabolic disorders during pregnancy are also involved in the genesis of postpartum depression [21]. Among the protective factors, evidence has demonstrated a key role for social support, including emotional support, financial support, intellectual support and empathetic relations [12]. Factors related to lifestyle, food intake patterns, sleep status, exercise and physical activity are also involved in the prevention of postpartum depression through direct and indirect effects on the level of serotonin in the brain [22].

During the first year after delivery, women with a psychiatric disorder are at the highest risk of psychiatric hospitalization [23]. Conversely, increased risk of severe postpartum psychiatric morbidity and substance use disorder was associated with severe maternal morbidity, with the highest period of risk extended to 4 months after hospital discharge [24].

Among women with a diagnosed mood disorder, the rate of relapse during the postpartum period is 30% for unipolar depression and 52% for bipolar depression or a

manic episode, whereas anxiety disorders are diagnosed in about 15% of women during pregnancy and about 10% of women postpartum [25]. Moreover, women who experience one episode of peripartum depression are at increased risk of recurrence with subsequent pregnancies, suggesting the need to assess and treat depressive symptoms early during pregnancy [26].

Alterations in many endocrine systems are present in pregnancy and the influence of endocrine changes on maternal mood and behaviour and fetal and child development has been widely investigated. Possible underlying mechanisms of maternal care alterations related to maternal depression include alterations in oestrogen and progesterone levels, central involvement of glucocorticoids in maternal care, altered hypothalamic-pituitary-adrenal axis function and the hypersecretion of cortisol [27-30].

A history of psychiatric disorders or onset in the peripartum period is one of the most important risk factors for suicidal behaviour. Depression in particular is a strong predictor of suicidality in the postpartum period [5, 6, 15, 31-37].

SUICIDE IN PREGNANCY AND POSTPARTUM

While being pregnant may actually protect against suicide, several subgroups of women may be at elevated risk before or after delivery [38, 39]. Even if suicide during pregnancy and postpartum is rare, it is among the leading causes of maternal perinatal mortality [39].

Suicidal behaviour encompasses a wide spectrum, from suicidal ideation (suicidal thoughts and plans) to self-harm, attempted suicide and completed suicide. Completed and attempted suicide are often preceded by suicidal ideation, which is therefore one of the main risk factors for completed suicide [40]. In addition, attempted suicide and self-harm are strong predictors for completed suicide [41]. During the peripartum period, the prevalence of suicidal ideation ranges from 5% to 14% [39, 42-43]. There is a strong association between suicidal ideation and depression. Most women with post-

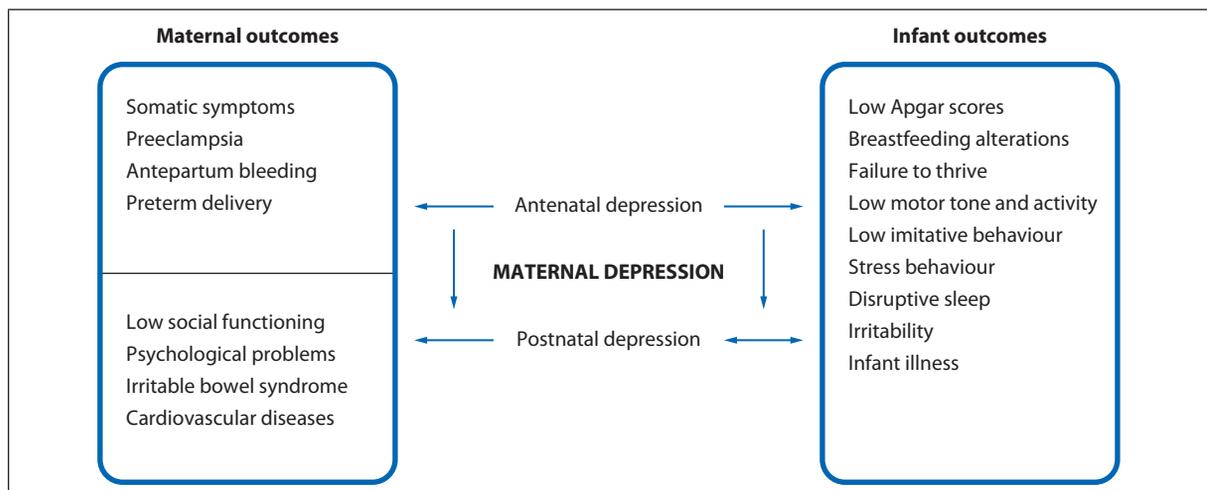


Figure 1
Most frequent aspects of peripartum depression.

partum suicidal ideation reported depressive symptoms and met the criteria for a major depressive episode [42-44]. Women who commit suicide during the peripartum period more frequently use violent and more lethal methods than suicidal women in other life periods, thus highlighting the greater intentionality of the act and the high level of psychopathology in these women [45-48].

Completed suicide as a cause of maternal mortality

According to the International Classification of Diseases (ICD) a “maternal death” is the death of a woman while pregnant or within 42 days of termination of pregnancy irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes. “Late maternal deaths” are the deaths that occur (from direct or indirect obstetric causes) more than 42 days, but less than 1 year after termination of pregnancy [49]. Comprehensive maternal death’ (introduced with ICD-11th revision) is a grouping that combines early maternal death (death of a woman while pregnant or within 42 days of termination of pregnancy) and late maternal death (death of a woman that occurs more than 42 days but less than 1 year after termination of pregnancy) [50].

The causes of maternal death are classified internationally according to the International Classification of Diseases for Maternal Mortality (ICD-MM) and are divided broadly into “direct” (pregnancy-related) and “indirect” (medical) causes. Antenatal and postpartum suicide are grouped according to the ICD-MM under “direct” causes of death (under the “other” category); this is recommended even if it may not be possible to definitively establish the diagnosis of puerperal psychosis and/or postpartum depression. Hence, maternal deaths due to suicide are identified when information about the pregnancy was indicated on the death certificate and are coded X60–X84 and Y97.0 according to the ICD [49-50]. One significant change with the introduction of the ICD-MM guidance in 2012 was the reclassification of maternal suicide from the indirect group to the direct group; however, this change seems to have had a minimal impact on the classification [51].

The fourth MBRRACE-UK annual report of the *Confidential Enquiry into Maternal Deaths and Morbidity* includes surveillance data on women who died during or up to 1 year after pregnancy between 2013 and 2015 in the UK and confidential enquiries into the care of women with severe postpartum mental illness and other physical or neurological conditions who died between 2013 and 2015 in the UK and Republic of Ireland; this report identifies suicide as the second largest cause of direct maternal deaths occurring during or within 42 days of the end of pregnancy and remains the leading cause of direct deaths occurring within 1 year after the end of pregnancy [52]. Suicide is reported as the second major cause of direct deaths occurring within 42 days of the end of pregnancy, after deaths by thrombosis and thromboembolism [52-53]. Furthermore, suicide represents about 18% of total deaths of women who died between 6 weeks and 1 year after the end of pregnancy in 2015-2017 [52, 53].

For the United States, Mangla *et al.* [54] report percentage suicides in the overall maternal mortality varying from 4% in Philadelphia, 5% in Texas and New York, 7% in Virginia and Illinois and a maximum of 13% in Colorado. In Ontario (Canada), suicide accounts for about 5% of the overall maternal mortality [55]. Lega *et al.* [48] found that for Italy, in the 7-year period 2006-2012, suicide deaths represent 12% of the deaths that occurred within 1 year from the pregnancy outcome. The Italian Obstetric Surveillance System (ItOSS) found that most suicides occurred between 43 and 365 days from the pregnancy outcome and suicide was the second cause of maternal death occurring 43-365 days following the end of pregnancy [48, 56].

Most maternal self-harm-related deaths occur in the late postpartum; a Canadian study found that the peak incidence period was between 9 and 12 months’ postpartum [55, 57].

Completed suicide during pregnancy and the 1-year postpartum period is estimated to be 3.7 per 100,000 live births in Sweden [58]. In the United States a peripartum suicide rate of 2.0 per 100,000 live births for 17 pooled states (South Carolina, Georgia, North Carolina, Virginia, New Jersey, Maryland, Alaska, Massachusetts, Oregon, Colorado, Oklahoma, Rhode Island, Wisconsin, California, Kentucky, New Mexico and Utah) was reported for the period 2003-2007 [59]. Another study that includes data for 50 states reports estimate suicide rates varying from 2.1 to 4.5 per 100,000 live births after adjusting for different hypothesized levels of misclassification (compared with 5.3/5.5 per 100,000 non-pregnant/non-postpartum women aged 10-54 years [60]. An even higher rate was reported for Colorado: 4.6 per 100,000 live births [57]. For Ontario (Canada), a perinatal suicide rate of about 2.6 per 100,000 live births was reported [55]. Knasmüller *et al.* [47] report, for Austria, a considerably lower rate of suicide amongst pregnant and postpartal women (0.89 per 100,000 birth events), probably attributable to a non-exhaustive identification of cases [47].

In Italy the peripartum suicide rate was 2.3 for 100,000 live births in 2006-2012 [48]; this is very close to the rate among the general Italian female population aged 15-49 years, which was 2.4 per 100,000 inhabitants in 2012 (our calculation using “Vital statistics on causes of death” data, collected by the Italian National Institute of Statistics and processed at the Italian National Institute of Health).

Risk factors for completed suicide during pregnancy and postpartum

Previous suicide attempts, self-harm, a history of psychiatric disorders before pregnancy, stressful life events during pregnancy and depression during the perinatal period have been identified as major predictors of suicidal ideation in multivariate analysis [42, 43]. Other factors involved in suicide risk in the peripartum period include previous abortion and unwanted pregnancy [1, 61, 62].

Completed suicide is characterized by impulsivity/aggression, depression, anxiety, hopelessness and self-consciousness/social disengagement [63], whereas low

self-directedness, low cooperativeness, higher anxiety and depression, lack of affection and anger and rejection towards the baby were found to be associated with suicidal thoughts [64].

Lysell *et al.* [6] found that mothers who died by suicide in the first year postpartum more often had affective disorders, psychotic disorders and a history of self-harm compared to living mothers.

Gold *et al.* [46] found that among the various risk factors, psychiatric symptoms, especially depression and substance abuse, were strongly involved in maternal suicide. Suicide risk was significantly elevated among depressed women during the entire peripartum period and it was found to be the second or leading cause of death in this depressed population [39]. In particular, it has been confirmed that a depressive status during the first 2 days' post-delivery predicted later suicidal ideation [65]. An important risk factor for completed suicide is the discontinuation of psychotropic medication during pregnancy [66, 67].

Suicidal ideation and suicide attempts are significantly higher among women with a diagnosis of depressive or bipolar disorder [39, 66, 68-70]. Furthermore, both suicidal ideation and suicide attempts are strong predictors of completed suicide. In women affected by minor depressive episodes, the prevalence of suicidality was reported to be about 34% during pregnancy and about 31% during the postpartum period [42].

Suicidal ideation and co-occurring postpartum depression share many of the same symptoms, although there are additional experiential aspects that can be detrimental to the mother and her relationship with the infant. Mothers who are suicidal can cognitively distort a small stressor into a lethal one. An overwhelming external stressor, such as pregnancy or the birth of a baby, can precipitate feelings of hopelessness and trigger thoughts of self-harm [71].

However, the association between depression and suicide is not deterministic. Zhong *et al.* [72] found that although the prevalence of suicidal behaviour was higher among those hospitalized with depression, more than 30% of hospitalizations were for suicidal behaviour without a diagnosis of depression.

It must be highlighted that suicide is a multifactorial phenomenon and a history of psychiatric illness is only one of the possible risk factors involved in suicide spectrum behaviour. Several psychological and social features contribute to increase the risk of suicidality during pregnancy and postpartum. These include, among others, sleep disturbance, stillbirth, undesired pregnancy, being abandoned by the partner, domestic violence, abortion or death of a previous child, lack of support, a history of psychiatric disorders, being unmarried and drug or alcohol abuse. In particular, women who committed suicide during the peripartum period were more frequently victims of domestic violence compared to suicidal women in the general population [46, 66, 73, 74]. Almost 50% of women died by suicide during pregnancy or within 1 year postpartum in Sweden from 1980 to 2007 had experienced adverse events during pregnancy [58].

On multivariate analysis, a history of suicide attempts remains strongly associated with suicidal behaviour

whereas social support and living with a partner remain protective factors [37].

The effect of maternal age on suicide in peripartum is not clear. Many studies report higher suicide rates after live birth and abortion in women younger than age 20 years compared with the same age group in the general population [5, 33, 37, 66, 72, 75-78]. Others studies found that women aged 40 years and over were more represented among suicide deaths during pregnancy, after delivery and after miscarriage [48, 59]. A list of the most important risk factors for suicide in the peripartum period is reported in *Table 1*.

Risk factors for fetus and newborn of mother's suicidality

Particular attention should be paid to the assessment of suicidal behaviour during pregnancy also for the consequences for the fetus and infant. Schiff and Grossman [79] demonstrated that fetal or infant death in the first year after delivery was strongly associated with hospitalization for attempted suicide in women.

Gandhi *et al.* [75] report that women who attempted suicide during pregnancy had increases in premature labour, caesarean delivery and need for blood transfusion, with analysis of neonatal outcomes revealing increases in respiratory distress syndrome and low birth weight; moreover, a sub-analysis that included women who delivered after hospitalization for attempted suicide demonstrated increased premature delivery, respiratory distress syndrome and neonatal and infant death. A list of the most frequent infant outcome of suicidal mother behavior in the peripartum period [80-84] is reported in *Table 2*.

In a clinical sample of mothers with postpartum depression, Paris *et al.* [84] found that mothers with high suicidality experienced lower maternal self-esteem, more negative perceptions of the mother-infant relationship and greater parenting stress. Women with high suicidality were less sensitive and responsive to their infants' cues and their infants demonstrated less positive affect and involvement with their mothers [84]. Moreover, postpartum suicidal ideation significantly correlated with thoughts of hurting the baby, which might lead to infanticide together with suicide [85]. Many mothers with postpartum depression experience shame and humiliation, viewing themselves as the worst mothers in the world and imagining that others also see them this way; such inner conflict can trigger suicidal thoughts for a woman who focuses on the idea that her baby would be better off without her or that she may hurt her baby if she lives.

It is well known that a family history of suicide is a risk factor for completed suicide. Moreover, in utero and perinatal conditions may contribute to increase suicide risk throughout the life span; thus, the effects of suicidal behaviour of the mother can also increase the suicide risk of children in adolescence or even older age [86].

Unrecognized and untreated postpartum mental illness can have tragic lethal consequences on the newborn. It has been reported that up to 30% of mothers who commit filicide also commit suicide [87]. Although

**Table 1**

Main risks factors for completed suicide in the peripartum period

Risk factors	References
Lifetime history or current diagnosis of depressive and anxiety disorders, major depression and other severe mental disorders (including psychosis)	Gelaye et al. 2016 [5]; Lysell et al. 2018 [6]; Oates 2003 [31]; Austin et al. 2007 [32]; Newport et al. 2007 [33]; Gavin et al. 2011 [34]; Coelho et al. 2014 [35]; Gressier et al. 2017 [36]; Martini et al. 2019 [37]; Gold et al. 2012 [46]
Psychiatric hospitalizations	Lysell et al. 2018 [6]; Gressier et al. 2017 [36]
Abrupt discontinuation of psychotropic drugs	Appleby et al. 1991 [66]; Orsolini et al. 2016 [67]
History of suicidal ideation and suicide attempts	Gelaye et al. 2016 [5]; Lysell et al. 2018 [6]; Martini et al. 2019 [37]; Lindahl et al. 2005 [39]; Beghi et al. 2013 [41]; Mauri et al. 2012 [42]
Lifetime or current history of substance use disorders, including alcohol and tobacco use	Oates 2003 [31]; Austin et al. 2007 [32]; Newport et al. 2007 [33]; Gressier et al. 2017 [36]
History of miscarriage and/or induced abortion	Coelho et al. 2014 [35]; Lega et al. 2019 [48]; Steinberg et al. 2019 [61]; Appleby 1991 [66]; Gissler et al. 1996 [78]; Mota et al. 2019 [96]
Stillbirth and infant death	Gissler et al. 1996 [78]; Schiff & Grossman et al. 2006 [79]
Unplanned/unwanted pregnancy	Gelaye et al. 2016 [5]; Newport et al. 2007 [33]; Frautschi et al. 1994 [62]; Appleby 1991 [66]; Kim et al. 2015 [77]
Low maternal education level	Gelaye et al. 2016 [5]; Newport et al. 2007 [33]; Gavin et al. 2011 [34]; Coelho et al. 2014 [35]; Gressier et al. 2017 [36]; Mauri et al. 2012 [42]; Alhusen et al. 2015 [74]; Gandhi et al. 2006 [75]; Pinheiro et al. 2012 [76]
Low household income and other adverse socioeconomic circumstances	Gelaye et al. 2016 [5]; Gavin, et al. 2011 [34]; Martini et al. 2019 [37]; Alhusen et al. 2015 [74]
History of abuse and intimate partner violence (including emotional abuse, physical and/or sexual violence) during pregnancy	Fisher et al. 2013 [25]; Coelho et al. 2014 [35]; Palladino et al. 2011 [59]; Halim et al. 2018 [73]; Alhusen et al. 2015 [74]
History of abuse/rape during childhood	Martini et al. 2019 [37].
Being unmarried/unpartnered	Gelaye et al. 2016 [5]; Newport et al. 2007 [33]; Martini et al. 2019 [37]; Gandhi et al. 2006 [75]; Kim et al. 2015 [77]
For pregnant teenagers: poor relation with parents (parental bonding: "affectionless control" and "neglectful parenting")	Coelho et al. 2014 [35]
Low social support	Gelaye et al. 2016 [5]; Palumbo et al. 2016 [12]; Coelho et al. 2014 [35]; Martini et al. 2019 [37]; Appleby 1991 [66]
Age 40 years and over	Lega et al. 2019 [48]; Palladino et al. 2011 [59]
Young maternal age (less than 20 years)	Gelaye et al. 2016 [5]; Newport et al. 2007 [33]; Martini et al. 2019 [37]; Appleby 1991 [66]; Zhong et al. 2016 [72]; Gandhi et al. 2006 [75]; Pinheiro et al. 2012 [76]; Kim et al. 2015 [77]; Gissler et al. 1996 [78]

Table 2

Main infant outcome of mother's suicidality

Infant outcome	References
Born early, preterm delivery, low infant birth weight; poor fetal growth, stillbirth, fetal death	Martini et al. 2019 [37]; Zhong et al. 2019 [72]; Gandhi et al. 2006 [75]; Czeizel 1992 [81]
Lower score for neuropsychological development	Martini et al. 2019 [37]
Long-term effect on child: increased risk of suicidality (transgenerational transmission of psychopathology and suicidality)	Sorenson and Rutter 1991 [82]; Orri et al. 2019 [86]
Depressive symptoms associated with suicidality can lead to lower maternal responsiveness, non-beneficial parenting behaviours, inadequate mother–infant interaction	Martini et al. 2019 [37]; Paris et al. 2009 [84]
Homicide death	Lysell et al. 2014 [83]; Naviaux et al. 2020 [88]

maternal infanticide is a rare event, a high proportion of cases occur in the context of postpartum mental illness. In particular, depression and psychosis represent very high risk factors for committing infanticide and neonaticide (when the neonate is killed within 24 hours after birth). It should be noted that fathers and mothers do not act the same way or for the same reasons when

they kill their offspring and neonaticide and infanticide are almost always committed by women [88]. Acute psychosis after childbirth is an important risk factor for infanticide [87] and severe anxiety and depression in pregnancy and postpartum can evolve into psychotic symptomatology [89, 90]. Psychiatrists have a vital role to play in recognizing the signs and symptoms of peri-

partum psychiatric disorders and in early identification and intervention with at-risk mothers [4, 91].

DISCUSSION

This broad overview sought to characterize completed suicide during pregnancy and in the peripartum period. We found that suicide during peripartum represents a leading cause of maternal mortality in the late postpartum. Overall suicide rates during the peripartum period do not seem to exceed the suicide rate among the general female population of reproductive age but for some susceptible groups of women pregnancy and postpartum can increase the suicide risk. Suicide remains a multifactorial phenomenon even in the peripartum. Depression and other severe psychiatric disorders are important, but not unique, risks factors for suicide; several demographic and social conditions combine to increase the risk of suicidal behaviour during the peripartum period.

Suicide prevention requires early screening, assessment, monitoring, and intervention for all women during the peripartum period, regardless of emotional affect and appearance. It is fundamental to investigate suicide risk, including suicidal ideation, thoughts, and intent, during pregnancy and the postpartum period, especially (but not only) in women affected by mental pathology.

Effects of maternal depression and suicide behaviour on infants range from physical and physiological to psychological and behavioural. Fetal growth has been found to be at risk when mothers suffer from depressive symptoms. Preterm deliveries and shorter gestations have also been associated with depressive symptoms. Furthermore, depressed mothers utilize preventative care for their children less often than non-depressed mothers and visit urgent care settings at a higher rate.

Systematic screening has been demonstrated to increase the identification of depression and to be more effective in identifying depression than clinical assessment alone [92]. Current guidelines from the United States Preventive Services Task Force and the Council on Patient Safety in Women's Health Care recommend screening women for depression at least once during pregnancy and/or after delivery [93, 94]. The American College of Obstetricians and Gynecologists (ACOG) recommends screening at least once during the peripartum period and recommends a postpartum screening even if screening took place during pregnancy [95]. All of these guidelines emphasize that screening alone is necessary but insufficient to address maternal depression, and providers must be prepared to initiate treatment or refer patients to mental health professionals when indicated.

It is important to implement and manage protocols for women at risk of serious psychiatric symptoms after childbirth in all maternal and neonatal wards. Information regarding psychiatric history should be collected routinely in order to investigate the presence of any familial psychiatric disorders. The term "postpartum depression" should not be used to indicate all possible mental disorders in the postpartum period because this may underestimate the gravity of the situation, as well as the consequent management. Psychosis and suicidal ideation in the peripartum period are relevant medical

emergencies that require immediate intervention.

Women who have a history of psychiatric disorders should be seen by a psychiatrist during pregnancy due to the high risk of relapse after childbirth, and women who have suffered from serious psychiatric conditions either after childbirth or in other phases of life should be informed about the possibility of relapse after subsequent pregnancies. In particular, women who have a history of bipolar disorder or postpartum psychosis have a very high risk of relapse after childbirth, thus presenting a higher risk of suicide.

Moreover, it has been reported that, compared with a non-perinatal period, the rate of a diagnosed mental disorder is lower during pregnancy but it rises in the postpartum period, highlighting the importance of early identification of women at risk [96]. Considering the high risk of infanticide, specific screening for severe psychiatric disorders should be performed routinely in obstetric and primary care [97, 98].

Available screening instruments for the peripartum period, such as the Edinburgh Postnatal Depression Scale (EPDS), are primarily designed to identify perinatal depression or psychiatric disorders [72]. Item 10 in the EPDS is used to identify women with suicidal thoughts or behaviour and the EPDS is a useful tool for this purpose. Nevertheless, considering the burden of suicide in this life period, an effort to develop a specific screening instrument would be of vital importance [15, 37].

The high prevalence of suicidal ideation among women without a psychiatric history of mental disorders highlights the importance of screening all women and carrying out a psychosocial assessment: psychiatric history, social support, domestic violence, etc. [43].

General practitioners, gynaecologists, midwives, paediatricians and psychiatrists need management training courses and knowledge of peripartum risk factors. Screening through validated tools on previous psychiatric disorders, history of domestic violence and the other risk factors listed above should be carried out routinely, as is done, for example, for diabetes and hypertension. It is therefore essential to invest in the training of health professionals (general practitioners, gynaecologists, paediatricians, nurses, midwives, psychiatrists) for the early recognition of risk factors in the field of perinatal mental health and for the identification of suicidal risk.

Suicidality should be assessed repeatedly by health professionals asking the woman at risk if she feels that life is not worth living or she wants to die or make suicide plans [37, 42]. Furthermore, specific care must be provided when suicide risk is detected, also in order to prevent infant harm [37, 42].

Providing long-term support of women at particular risk may reduce self-harm and suicide mortality and also improve the well-being of the newborn, the father and the whole family network.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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A structured program for perinatal depression and anxiety to be adopted in the emergencies

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Abstract

Quarantine, loss of routine and social support can negatively impact mothers who have just given birth and their babies, generating concerns and reactions of intense fear. Following the COVID-19 emergency, we described a structured program for screening and treatment of perinatal depression and anxiety as a medium for constant monitoring of perinatal risk factors and early screening, which can also be implemented in emergencies with remote intervention methods, to offer women an appropriate, timely and effective treatment. In this scenario, it is desirable that the monitoring of the psychological well-being of women in postpartum is maintained over time, with the participation of all the professional figures with whom the woman comes into contact, to intercept any forms of psychological distress related to the epidemic and that could occur even after some time.

Key words

- screening
- treatment
- depression
- anxiety
- perinatal mental health

INTRODUCTION

The emergency created by the COVID-19 pandemic is having a deep impact on all aspects of society, including those concerning mental well-being [1]. Many factors can influence a person's psychological well-being: the presence of a real threat of disease for oneself or others, isolation, physical distance, modification of daily habits, loss of work routine, and an overabundance of inaccurate and contradictory information. Several studies have shown that, in the event of an extraordinary epidemic, it is possible to expect an increase of anxiety symptoms in the population, a decrease in the ability to cope with stress and an increased risk of developing depressive symptoms and self and hetero-aggressive behaviours including suicidal risk [2].

However, women in the perinatal period constitute a population particularly vulnerable to the psychological effects of the pandemic [3]. It is common for pregnant women and new mothers to experience mood swings and emotional changes mainly due to hormonal alterations and the perceived load of maternal responsibility. Generally, this emotional state tends to resolve itself, but psychological difficulties or real mental disorders can emerge and consolidate [4-6]. During the perinatal period, this situation can have large-scale repercus-

sions because the well-being and mental health of the mother, father and child are closely related [7]. In fact, it is well known that the emotional difficulties of parents can interfere with the parent-child relationship, with negative consequences on the child's cognitive, social and emotional development [6, 8-10]. Perinatal clinical psychology studies [11] clearly show how the mother-father-infant relationship affects the construction of the neuropsychic structure of the baby's brain, especially during the perinatal period and, to some extent, throughout life [12]. Furthermore, the psychological distress and psychiatric disorders that emerge in women in the perinatal phase can be associated with the impoverishment of the quality of the relationship in the family and with the poorness of the emotional, intellectual and cognitive development of the child [13, 14]. In addition, this is exacerbated by the already high treatment costs that national health systems face [15].

The COVID-19 studies available to date suggest that pregnant women and their children are not at a greater risk of contracting the infection or having severe symptoms or consequences than the population as a whole [16]. Moreover, the evidence currently available shows no evidence that the virus can be transmitted vertically [17] and it is clear, in the light of the knowledge avail-

able so far, that infants and children who become infected have a milder disease course and a better prognosis than adults [18].

However, quarantine, loss of routine and social support can negatively affect mothers who have just given birth and their babies. Recent studies that have taken into consideration past epidemics have shown that quarantine generates concerns and reactions of intense fear, particularly in women who are pregnant or have just given birth [2]. Overall, quarantine was associated with high levels of stress [19-22], depression [23], irritability and insomnia [24] and increased risk of suicide [25-27]. A recent Italian study highlighted how the prevalence of anxiety and depression in the perinatal period is higher in women who gave birth during the lockdown period in a "COVID-19 hotspot" hospital compared to women who gave birth in the same hospital a previous year [28]. Studies in countries other than Italy have confirmed these data [29, 30].

As a result of the containment policies of the COVID-19 pandemic, direct access to health and care services dedicated to health (and in particular to mental health) has been limited only to emergencies, thus making it difficult to accommodate the requests of the population and increasing the risk of suffering [31]. Telephone contacts, video calls, messages have partly made up for this deficiency [22] but it should be noted that these forms of contact require intentionality, while in non-emergency times contacts also occur casually and, in the event of any problems, the parental and friend networks (when present and able to act as support networks) can intervene to provide support and help.

Women who have experienced pregnancy or childbirth during the COVID-19 pandemic, with the usual fears and anxieties, may have experienced the fear of contagion, concerns about their own health and the health of their children and loved ones, fear of isolation, of being subjected to obstetric-gynaecological procedures (ultrasound, visits...) completely in solitude, uncertainties related to the choice of the hospital where to give birth, finally, fear of having to give birth in isolation without the support of the partner [31].

Furthermore, women and children may be more affected than others and may be forced coexistence within the home. Where families are more closely connected and spend more time together, the likelihood that women and children are exposed to violence increases, especially if there are serious economic or job losses in the family; as resources become scarcer, forms of partner abuse, power and control can also increase [32-35].

Finally, among the effects of the COVID-19 emergency, is likely an increase in alcohol consumption, especially in the medium and long term [36], defining itself not only as a direct risk factor for suicide but also an indirect one because of possible triggers of domestic violence. In this scenario, it is therefore crucial to identify and support women at risk of perinatal anxiety and depression early on.

The goal of this article is to describe a structured screening and treatment program for anxiety and depression in the perinatal period, to be adopted in

times of emergency. This program is an adaptation of a broader and more articulated program, for which effectiveness has been demonstrated through a study promoted by the Istituto Superiore di Sanità in 2015 [37] which is carried out in the traditional ways of physical co-presence of the woman and the therapist in the same place, useful to be used in non-emergency periods when physical presence and proximity between people are allowed.

A STRUCTURED EVIDENCE-BASED INTERVENTION PROGRAM FOR THE MANAGEMENT OF PERINATAL MENTAL HEALTH

This program has proved to be suitable for getting the psychological distress of mothers and fathers during the perinatal period and useful for prompt intervention, containing any damage that the chronic aspect of the disease can bring to the woman, the child, their relationship, and to the family atmosphere.

The program is currently active, as well as in various services in the Veneto and Lombardy, also in many services in different Italian regions, belonging to the Operating Units of the Perinatal Clinical Psychology Observatory of the University of Brescia [38]. Similar programs are active at the Italian university centres belonging to the Multicentric Perinatal Depression Observatory (OMDP) (www.ptvonline.it/uo_ginecologia.asp#sos) located in the Lazio, Sicily, Puglia, Campania, Abruzzo, Marche, and Trentino-Alto Adige Regions.

The basic requirement of the program is the specific training of the personnel involved, based on theoretical and applicative knowledge that can be used effectively in daily clinical practice but also a personal ability to know how to establish a familiar, empathic, welcoming, non-stigmatizing climate so that women recognize their difficulties and accept to be helped.

The fundamental phases of the program are the empowerment of the knowledge and information of women and family members on psychological disorders in the perinatal period, the screening, the assessment, the treatment and the follow-up of the effects of the treatment.

AN ADAPTATION OF THE INTERVENTION PROGRAM DURING THE COVID-19 PANDEMIC

The emergency created by the COVID-19 pandemic and the need to take measures to contain the infection, such as movement restrictions and physical distancing, have forced the Services to review procedures to continue providing pregnant women with quality care, ensuring safety for users and operators.

The structure of the Program

The *empowerment* of knowledge is the first phase of the program, which involves raising awareness of women on the problem of perinatal mental health and proposing screening. This action can be undertaken during the birth preparation courses even remotely, or through information material specially prepared, on the occasions of necessary contact (family health facilities,

hospital wards, paediatric visits), during pregnancy on the occasion of morphological ultrasound (19-22 gestational weeks), after delivery when the new-born is first vaccinated (45-60 days of life) and during the paediatric visits. Women willing to take part in the program are asked to sign the privacy policy and an informed consent form. The consenting process can be achieved face-to-face or remotely, via smartphone app or email.

All professionals (gynaecologists, midwives, general practitioners and paediatricians) who meet the women both before and after childbirth can perform the *screening*, for the identification of the anxiety-depressive risk. The actions of this phase consist in the collection, within a general interview on the mental health and well-being of the woman, of the socio-demographic data and in the administration of questions on the identification of depression and anxiety recommended by the National Institute for Health and Care Excellence (NICE) [39].

Questions about depression:

- *During the past month, have you often been bothered by feeling down, depressed or hopeless?* (dichotomous Yes-No scale);
- *During the past month, have you often been bothered by having little interest or pleasure in doing things?* (dichotomous Yes-No scale).

Questions about anxiety using the 2-item Generalized Anxiety Disorder scale (GAD-2):

- *Over the last 2 weeks, how often have you been bothered by feeling nervous, anxious or on edge?* (4-level Likert scale: 0 to 3);
- *Over the last 2 weeks, how often have you been bothered by not being able to stop or control worrying?* (4-level Likert scale: 0 to 3).

In case of clinical suspicion (positive answer to one of the first two questions on NICE depression, or, in case of a score equal to or greater than 3 to the sum of the answers to the two questions on GAD-2 anxiety), the woman is invited and accompanied to carry out an assessment and to undertake a path of psychological support.

A psychologist or a psychiatrist carries out the subsequent *assessment* of the woman who meets the criteria indicated above regarding the four questions by NICE. In particular: if the woman reports at least one positive response to the two questions on depression, it is necessary to investigate with the Edinburgh Postnatal Depression Scale (EPDS) [40-41]; if the sum of the answers to the two questions of GAD-2 is equal to or greater than 3, then it is necessary to further investigate with the Generalized Anxiety Disorder Scale (GAD-7) [42]. Administration of these tests can be performed remotely. It is also possible to send the EPDS and the GAD-7 in Word format via email, eliminating the coding of the answers, preferably arranging them so that the woman can freely answer each question, without being conditioned by the numerical value associated with each answer.

In addition to the two tools mentioned, it is appropriate and necessary to carry out an anamnestic investigation through an assessment form on psychosocial risk factors prepared and validated by the Istituto Superiore di Sanità [43, 44], aimed at acquiring information relat-

ing to pregnancy and childbirth, other possible experiences of depression or psychiatric problems in life, any stressful events in the last 12 months, perceived family and social support.

The psychologist/psychiatrist returns the evaluation information by telephone, possibly within 3 days, and agrees with the woman on the program to be implemented. It is also possible to offer a face-to-face interview to women who have high levels of depression or anxiety in the tests, naturally respecting the recommended measures to limit the spread of the epidemic. What is described in the original intervention program regarding the assessment of suicide risk remains unchanged.

The *treatment* is based on the model of proven experimental efficacy developed by Jeannette Milgrom and her team [45] at the Australian Parent-Infant Research Institute (PIRI®) of the Heidelberg Repatriation Hospital [46, 47]. The most recent evolution of this model is the *MumMoodBooster* version, online treatment for postpartum depression, which is equally effective [48, 49]. This treatment has not yet been adapted to the Italian reality; however, many Services have reorganized themselves by offering a way of contacting women remotely, using the technological means available to the person. In particular, the processing was carried out both individually and in groups (four to five people) using online communication platforms. The part relating to the mother/child relationship, usually entrusted to the midwives and educators of the family health facilities, can be activated as online consultation. Where necessary or required, in compliance with national directives, there remains the possibility of face-to-face meetings or home visits.

Also, in this emergency phase intervention program, at the end of the treatment period, the women are again subjected to evaluation with the tools used in the clinical study phase (*follow-up*). Women who still have high-risk values (equal to or higher than the cut-offs) at the assessment are accompanied and supported in taking charge by psychiatric services or family health facilities, also through periodic home visits, depending on the organization local service, observing the precautionary recommendations, such as safety distance and use of personal protective equipment.

CONCLUSIONS

The program described representing an early screening and treatment tool for perinatal depression and anxiety helpful to be used in emergencies with remote intervention modalities, to offer women an appropriate, timely and effective intervention.

It is therefore in line with the recommendations of the WHO, that has highlighted the need for "evidence-based, cost-effective, and human rights-oriented mental health and social care services in community-based settings for early identification and management of maternal mental disorders" [50].

Besides, the recent survey undertaken by WHO in 130 countries provides the first global data showing the devastating impact of COVID-19 on access to mental health services and emphasized that the COVID-19

pandemic has disrupted or halted critical mental health services in 93% of countries worldwide while the demand for mental health is increasing [51].

It is therefore particularly urgent to implement programs, such as the one described, to monitor the mental health of women in the peripartum and be ready with an effective intervention in case they need support.

Furthermore, the activation of perinatal mental health screening programs and the launch of information campaigns, not only through consultants and hospital wards, but also through general practitioners, pediatricians and health professionals of vaccination centers are particularly crucial for early intercepting any forms of psychological distress related to the experience of the epidemic and which could occur even after some time.

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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QUALITY OF CARE FOR PEOPLE WITH CHRONIC DISEASES: ENGAGED IN COLLABORATION, ACHIEVING RESULTS

Edited by Marina Maggini, Bruno Caffari and Jelka Zaletel

Preface

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Reducing the burden of chronic diseases such as diabetes, cardiovascular disease, cancer and mental disorders is a priority for decision-makers and leaders in health care all over Europe, since they affect 8 out of 10 people aged over 65 in Europe.

There is a great potential for reducing the burden of chronic disease by using existing knowledge in an effective and efficient way promoting policies and practices that have proved successful in the past. Sharing of tested policies and practices, through cross-national initiatives across European countries, is the core idea that has driven Joint Action CHRODIS PLUS – Implementing good practices for chronic diseases – during its 39 months of operation (www.chrodis.eu). It was the second Joint Action, co-funded by the Health Programme of the EU, dealing with chronic diseases, which brought together over 50 partners from 21 European countries. This initiative was a multinational knowledge transfer of tools and evidence-based practices developed in the first Joint Action CHRODIS on chronic diseases and promoting healthy ageing across the life cycle (chrodis.eu/outcomes-results/).

CHRODIS PLUS, through its professional scientific network and motivated implementers across EU, raises awareness of the notion that in a health-promoting Europe, free of preventable chronic diseases, premature death and avoidable disability, policies and practices on chronic diseases should build mainly on prevention, patient empowerment and a high quality of care for people with chronic diseases. To achieve these goals, health and social care systems have to facilitate the transition from fragmentation to integration of care, including prevention efforts, and incorporating community resources, in order to ensure a seamless care coordinated with and around the needs of people with chronic diseases. Moreover, joint efforts and sustained commitment to address major chronic diseases could help to decrease inequalities in health within and across European countries.

Within the Joint Action CHRODIS PLUS, twenty-

one implementation projects were developed (www.chrodis.eu), eight of them aimed to foster high quality care for people with chronic diseases through the implementation of a set of Quality Criteria and Recommendations (QCR tool) [1, 2]. These criteria are the result of a structured methodology involving representatives of patients and experts from a wide number of organizations across Europe and from a variety of professional backgrounds. QCR tool was put forth to improve prevention and quality of care of diabetes (case study) but it's general enough to be applied to any of the chronic diseases, and may be applied to various domains, e.g. prevention, care, health promotion, patient education, and training for professionals. Moreover, it can be used in countries all across EU, irrespective of political, administrative, social and health care organization. The tool is supportive towards assessing whether an intervention, policy, strategy, program as well as processes and practices, can be regarded as a “good practice” in the field of chronic disease prevention and care.

QCR tool was used as a framework for practice development, implementation, monitoring and evaluation by partners from eight European countries. In this issue of *Annali dell'Istituto Superiore di Sanità* four papers report experiences and results of interventions addressing the use of QCR in Croatia, Finland, Serbia and Slovenia.

In Croatia the project aimed to improve general practitioners' awareness and practice in diabetes monitoring, to improve patients understanding regarding the importance of yearly check-ups, and to harmonize diabetes information systems and coordination mechanisms with professional standards at the international level. Twenty-eight general practitioner and 1242 diabetic patients were included. General practitioners were randomized in three groups receiving different level of education and feedback. Qualitative and quantitative methods were used [3].

The project in Finland created and tested a culturally sensitive lifestyle intervention model among a hard-to-reach and underserved population, specifically people

with immigrant background. Specific objectives were to increase awareness on risk factors and prevent type 2 diabetes, and to improve health and wellbeing among this population. Despite the intervention was focused on people with a Somali immigrant background who reside in Helsinki, the implementers suggested that the model could be adopted in other settings but would require close collaboration with the respective target population and providing expert training to the local implementers [4].

Redesigning health care delivery to achieve better coordination of services was the objective of Serbian project. The intervention led to the establishment of the National Diabetes Centre as reference institution, which is now the coordinating centre for diabetes care and education in Serbia. Diabetes Care Units were re-introduced at the primary care level. The implementation of stepwise protocols for identification of patients at high risk for T2D or with previously undiagnosed T2D leads to establishment of a systematic approach to these patients. The regular educations for physicians and nurses, created opportunities to improve knowledge and everyday practices, as well as to create a uniform approach to diabetes care in the entire Country [5].

In Slovenia a model was developed to integrate care across levels of healthcare and the community to address the challenges of multidimensional care for people with complex chronic conditions. The model was developed based on a case study of chronic wound by mapping out structures, processes, barriers and enablers to integrated care in close collaboration with patients and relevant stakeholders in health care, social care and within community. The practice focused particularly on enhanced patient participation and on the sustainability of the practice through community partnership and

support of the national policymakers [6].

QCR usability was tested and evaluated in projects designed and carried on in different health care systems, in different contexts and addressing different scopes, and mostly resulted in implementation of complex changes in healthcare. There was a consensus among implementers that QCR tool was a positive framework which supported their projects, also establishing high level of involvement of target population, showing a great potential for sustainability and scalability.

A valuable learning point is that all implementation working groups consider QCR tool as a trusted source of strategy and procedures when it comes to the design, development, and implementation of practices and activities onto their respective sites, highlighting that implementing change is most effective when aligned with local priorities. Trust is the best way to make stakeholders work together in order to provide an improved quality of life for those with chronic diseases.

A striking characteristic of the implementation projects has been the enthusiasm and hard work observed at all of the sites, and the willingness of stakeholders (health professionals, decision makers, patients and their representatives) to cooperate and learn from the oversight team: learning from their own experience; sharing experiences with other work groups; learning from the experiences of other countries. Partners themselves represent a knowledge hub and a network with hands-on expertise in improving prevention and care of chronic diseases.

Sharing and discussing experiences is an effective means to set up a capital of knowledge that can also be used in the future, the added value is represented by the creation of a network, a community, a transnational human capital that does not end with the end of the specific projects.

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Croatian diabetes registry (CroDiab) and implementation of standardised diabetes checklists using Joint Action CHRODIS Recommendations and Criteria

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Abstract

Introduction. Standardized diabetes monitoring checklists is an efficient registry collection tool and diabetes care improvement aid. Aim of this study was to improve the management of diabetes according to international standards and based on Joint Action CHRODIS Recommendations and Criteria, and to improve general practitioners (GPs) awareness of importance of monitoring via diabetes checklists.

Population and methods. Twenty-eight GPs and 1242 diabetic patients were included. GPs were divided in groups regarding the intensity of education and information provided. Quantitative analyses of diabetes quality indicators and their availability as well as qualitative study in intensive group were performed.

Results. Average number of patients with fulfilled checklists per GP increased from 20.2 to 30.8 (52.30%). Most GPs had positive attitude towards checklists but there is still a room for further improvement.

Discussion and conclusions. Checklists are perceived as positive initiatives by GPs; however, there are areas for further improvements. General practitioners education and feedback regarding the checklists may contribute to better monitoring of patients with diabetes.

Key words

- diabetes
- registry
- quality improvement
- quality indicators

INTRODUCTION

Diabetes is one of the major public health problems worldwide and it is estimated that there were 463 millions of people with diabetes in the world in 2019 and that till 2045 that number will increase for more than 50% to 700 million people [1]. It is known that diabetes registries can serve to interventional purposes and are proven to be efficient in quality improvement through implementation of standardized minimum data set i.e. diabetes checklists [2-4].

Diabetes registry in Croatia has a long tradition [5, 6], and during the time, the collection mechanisms have changed from paper-based reports to collection of existing electronically based data. With the change of medical documentation in primary health care setting from predominately paper based to electronically based data in certified platforms, we were also faced with the chal-

lenge of incorporating electronic diabetes checklists into the daily routine of general practitioners (GPs). Studies performed in Croatia confirmed that diabetes checklists are efficient in quality improvement in national settings [7, 8] so since 2014 checklists became a part of GPs official application for medical and financial documentation toward National Insurance Fund. Data are then transferred to Croatian Institute of Public Health, holder of diabetes registry. Even though checklists were available since 2014 in their current format, and reporting was stimulated from the National Insurance Fund and Croatian Institute of Public Health, checklists are still not completely implemented and only one third of all diabetes patients are monitored [9].

Aim of this study was to improve the management of diabetes according to international standards and based on JA CHRODIS Recommendations and Criteria (QCR

tool)(chrodis.eu/wp-content/uploads/2020/10/short-guide-for-the-implementation-of-good-practice_nijz.pdf). Specific aims were to improve general practitioners' awareness of importance of monitoring via diabetes checklists, and to improve their practice in monitoring as well as recognize obstacles in current implementation and area for potential future improvement.

POPULATION AND METHODS

Participants and study design

The study was planned with the help of QCR tool. During the practice design, the tool was used to specify study aims, objectives and methods, but also to clearly define target population. The tool emphasized importance of multidisciplinary approach and linkages across all relevant decision makers and stakeholders and was used to create diverse local implementation working group (LIWG) which consisted of representatives coming from different fields and institutions (Ministry of Health, Croatian Health Insurance Fund, patient representatives, GPs representatives). Sensible selection of working group members was probably the most important part of the project and it greatly contributed to the sustainability of the practice.

Primary target population were general practitioners which provide primary healthcare services to people with diabetes. People with diabetes were included directly in interventions via diabetic patient association and through distributed leaflets, which were intended for patient education about importance of yearly check-ups. GPs empowerment was planned through education about importance and meaning of diabetes checklists usage.

We included 28 randomly selected GPs allocated in one of three groups: group 1 or "intensive group" received information regarding the study and study protocol, education on registry and checklists, and analysis of their patients' quality indicators monitored in the 2018, and they were also interviewed; group 2 or "medium group" received e-mail with information regarding the study as well as study protocol and results of their patients' quality indicators analysis monitored in the 2018; group 3 or "no intervention group" did not get any information regarding the study.

Data were monitored as a part of regular monitoring of diabetes quality indicators by Croatian Institute of Public Health.

Interviews

We used semi-structured qualitative interviews before and after education about different aspects of checklists including questions regarding diabetes quality indicators, general impression on checklists, checklists usage in everyday work, barriers in everyday usage, necessity of a feedback, motivation for fulfilling checklists, area for improvement, general comments on checklists.

Open predefined questions were as follows: What is your opinion regarding the diabetes checklists? What do you think regarding indicators included in the checklists? How do you use them in your everyday practice? What do you think aggravates work with checklists? What are your suggestions for improvement? Do you

think that feedback regarding the data is good and necessary? What motivates you to fulfil the checklists? Do you have additional comment or suggestion?

After six months GPs were also asked to give additional comments on checklists if there were any besides the facts reported in the first interview.

Analyses

We used qualitative and quantitative approach for analysing our data. Quantitative analyses have been used to track changes in GPs baseline performance, measured by share of persons with regularly completed checklists. Additionally, quality of checklists completeness and change of chosen diabetes quality indicators within checklists were measured.

GPs were informed that we were going to analyse quality indicators of their patients in preceding period and compare same trimester of 2018 to 2019 data in order to evaluate percentage of patients with fulfilled diabetes checklists and differences in the main quality indicators (QI). Analysed quality indicators were as follows: body mass index, systolic blood pressure, diastolic blood pressure, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, fasting glucose, HbA1c, smoking status and alcohol consumption. After six months, researchers contacted GPs by e-mail and phone and presented trend in results of their patients.

Statistical analyses were performed using SPSS (version 21). Normality of distribution was tested using Shapiro-Wilks test, while homogeneity of variance was tested using Levene test. Differences between groups of independent continuous variables were analysed using One-way and Welch's ANOVA. Tukey's HSD and Games Howell test were used for post hoc analysis. Differences before and after intervention were analysed using t-test and Wilcoxon matched paired test for dependent measurement. An error threshold of $\alpha = 0.05$ was used in the interpretation of the results. Interviews were audio recorded, transcribed verbatim, and content was analysed inductively. Two researchers performed qualitative analysis.

RESULTS

Total number of patients included in quantitative analysis was 1242, i.e., 566 patients with fulfilled checklists in Jul-Oct 2018 and 862 patients with fulfilled checklists in Jul-Oct 2019. Average number of patients with fulfilled checklists per general practitioner was 20.2 in Jul-Oct 2018 and 30.8 Jul-Oct 2019 (total increase 52.30%). In group 1 patients with fulfilled checklists per general practitioner were 13.0 in Jul-Oct 2018 and 28.8 Jul-Oct 2019 (increase 121.15%); 27.5 vs 33.5 patients (increase 21.82%) in group 2; 18.7 vs 29.7 patients (increase 58.82%) in group 3.

Description of chosen quality indicators as well as differences between groups in 2018 and 2019 are presented in *Table 1*.

Before intervention there were no differences between groups in body mass index, diastolic blood pressure, low-density lipoprotein, high-density lipoprotein, triglycerides, smoking and alcohol status (all $p > 0.05$); while systolic blood pressure ($p = 0.048$; group 1 vs

Table 1

Differences in the main diabetes quality indicators according to groups before and after intervention. Group 1: intensive intervention; group 2: medium intervention; group 3: no intervention

	2018				2019			
	Group1	Group2	Group3	p	Group1	Group2	Group3	p
BMI	30.37 + 6.53	30.14 + 5.10	30.13 + 5.65	0.931	30.31 + 5.67	29.39 + 4.87	31.71 + 6.39	<0.001
SBP	138.79 + 14.93	135.14 + 13.78	134.02 + 16.83	0.048	135.87 + 15.63	134.10 + 12.42	135.65 + 15.14	0.297
DBP	79.97 + 8.30	80.81 + 6.36	80.11 + 8.53	0.554	79.36 + 8.09	79.58 + 7.10	80.47 + 8.90	0.258
TC	5.18 + 1.10	5.32 + 1.40	4.96 + 1.26	0.025	5.32 + 1.36	5.48 + 3.35	5.00 + 1.21	0.049
LDL	3.10 + 0.93	3.21 + 1.05	2.94 + 1.08	0.059	3.15 + 1.05	3.28 + 1.85	3.07 + 1.09	0.258
HDL	1.31 + 0.37	1.27 + 0.37	1.31 + 0.35	0.650	1.28 + 0.36	1.29 + 0.34	1.32 + 0.36	0.297
TG	1.76 + 0.90	2.04 + 1.04	1.86 + 1.14	0.069	2.07 + 1.84	1.96 + 1.24	1.82 + 0.89	0.124
HbA1c	7.23 + 1.40	7.53 + 1.49	7.37 + 1.48	0.270	7.12 + 1.16	7.36 + 1.31	7.19 + 1.31	0.126
Smoking (%)								
yes	12.50%	15.68%	18.86%	0.442	15.28%	18.95%	22.99%	<0.001
no	76.04%	73.73%	66.86%		62.04%	72.28%	63.60%	
ex	11.46%	10.59%	14.29%		22.69%	8.77%	13.41%	
Alcohol use (%)								
yes	20.22%	16.11%	28.30%	0.390	27.32%	16.03%	27.27%	0.003
no	79.78%	83.89%	71.70%		72.68%	83.97%	72.73%	

Data are presented as mean ± standard deviation and percentages. BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, LDL = low-density lipoprotein, HDL = high-density lipoprotein, TG = triglycerides.

group 3) and total cholesterol ($p = 0.025$; group 2 *vs* group 3) differed significantly. After intervention there were significant differences between groups in body mass index ($p < 0.001$; group 1 *vs* group 3 and group 2 *vs* group 3), smoking ($p < 0.001$), alcohol consumption ($p = 0.003$) and total cholesterol ($p = 0.049$; group 2 *vs* group 3). There were no differences between groups in other parameters (all $p > 0.05$).

Among all patients, only 161 of them (group 1, 24; group 2, 97; group 3, 40) had completed checklists, both before and after intervention. When analysing differences in selected quality indicators we observed statistically significant increase in total cholesterol and low-density lipoprotein levels ($p = 0.001$, $p = 0.003$) in all groups (group 1 $p = 0.002$; 0.006, group 2 $p = 0.009$; 0.019, group 3 $p = 0.015$ and 0.014). There were no statistically significant changes (all $p > 0.05$) in other indicators.

There were not enough data regarding waist and hip circumference and urine albumin/creatinine ratio as well as feet examination and funduscopy so in qualitative analysis we aimed to explore availability of that indicators too. Analysis revealed that waist and hip circumference are not perceived as important, urine albumin/creatinine ratio is not available on the primary level and also general practitioners were not aware that if they record feet examination and funduscopy it would not be recorded as self-performed intervention.

The qualitative research confirmed that most of GPs have positive attitude towards checklists, which can serve as reminders in regular monitoring of people with diabetes. This is how one of the GPs described checklists and their use: "So, it is just a help...something that I

need to check with my patients with chronic condition anyway... Yes, it is exactly checklist or suggestion. For me it is organisational reminder..."

Besides general attitudes towards checklists, the analysis identified seven themes that represent the baseline for future improvement of checklists and their implementation and even more important for diabetes care on the primary level. Themes were as follows:

- *Albumin/creatinine index on primary health care level.* GPs were aware of importance of early screening of diabetic nephropathy; however, they all underline that albumin excretion in 24h urine is currently only available test in hospital setting and it is associated with very low compliance of patients. Alternative is measuring albumin/creatinine index again only in nearest hospital, but that possibility is also not convenient for all patients with diabetes in routine monitoring on primary health care level. That all leads to occasional screening of diabetic nephropathy and GPs believe that albumin/creatinine index can be efficiently used in their patients, that this is appropriate index and the activities for their implementation in primary laboratories are needed;
- *Regular checklists feedback to GPs.* All participants had positive attitude towards feedback that included analysis of their patients' indicators and comparison with Croatian average. They find it very useful since that implies that data are not just collected but are really used for public health interventions and improvement of diabetes health care. Furthermore, they believe that feedback can additionally motivate them to use checklists and overcome gaps in monitoring patients with diabetes;

- *Involving nurses in checklists work.* In Croatia primary health care team consist of physician and nurse, with physician being team head. Administratively it implies that the National Insurance Fund recognizes activities performed by physicians and presumes that only administrative work and nursing care is in the nurses' domain. However, GPs believe that nurses are very efficient and qualified and can coordinate and perform monitoring with, if needed, consultation with GPs. That is why they believe it would be beneficial if National Insurance Fund could reduce the administrative workload for nurses and officially recognize monitoring via checklists as nurses' activities too;
- *Reducing the number of indicators.* Participants feel that list of indicators is too extensive. Even if indicators are important, GPs see them as a burden if the list is long. They recommend that list should be shortened and include only available and most important indicators if the coverage of complete diabetic population is priority. By reduction of list to essential indicators, compliance of GPs could be increased;
- *Improvement of application.* GPs see as a redundant work some of the activities with the checklists. Electronically enhanced copying data from other sources and archive data (previous checklists, hospitals) and possibility of overview/browsing including alerts about possible absence of yearly check-ups on all patients with diabetes are adjustments that can further facilitate utilization of checklists;
- *Financial stimulation.* GPs that are health care centres employees and are paid through fixed salaries are not financially stimulated, as are private practitioners for fulfilling the checklists. GPs believe that this situation is discouraging and that additional stimulation from the management of health centres is essential;
- *Additional funding.* Although GPs strongly state that financial aspect is not their main motivator, they suggested that the National Health Insurance Fund should increase funding, not just symbolically as is now the case. They believe that this could increase the proportion of persons with regularly completed checklists.

DISCUSSION

Results of this study revealed increase in average number of patients with fulfilled checklists per general practitioner. Increase was the highest in intervention group as expected; however, in medium group we observed lower increase than in no intervention group. Greatest increase in group 1 can be explained with influence of provided education and interviews while lowest increase in group 2, we believe might be result of negative feedback on checklists when participation in project were not discussed and accepted by participants, i.e., general practitioners were just informed that they will be monitored. This conclusion is emphasized by the results of qualitative analysis where some participants answered that checklists can be seen as a part of monitoring physician performance from Health Insurance Fund and they are not willing to provide the data that can enable that type of monitoring. It implicates that any intervention in

the area of checklists needs to be substantially communicated with GPs and their representatives.

Pre- and post-interventional indicators analysis did not reveal any significant improvement in the indicators value as expected from the previous national study [7]. It might be result of relatively small sample and short duration of the study that was determined by the duration of the project. Duration of the study is the main limitation of our investigation.

Qualitative analysis revealed areas for possible future improvements. Albumin/creatinine index is the parameter that needs to be accessed on the yearly basis in all patients with type 2 diabetes [10]. Since the organization of diabetes care for type 2 diabetics is primarily oriented on the primary health care level in Croatia, it is essential to enable this testing in the primary health care settings. Results of this study additionally confirmed that. Regular checklists feedback to GPs was also revealed as area for potential improvement. Previous studies on feedback on performance compared with usual care showed that the process of care improved by better prescription patterns and a better stimulation to follow the guidelines more closely and intensification of therapy so feedback can be one of the mechanisms to overcome clinical inertia in primary care settings [11, 12]. The results and observation of participants regarding the regular feedback was expected, and we believe that their recognition from GPs side will additionally reinforce feedback acceptance. Since multifaceted professional interventions and organizational interventions that facilitate structured and regular review of patients are effective in improving the process of care [13] involving nurses in checklists work seems to be expected request too. With addition of patient education to organizational interventions and the enhancement of the role of nurses in diabetes care we can expect improvements in patient outcomes and the process of care [13]. Qualitative analysis also revealed number of quality indicators as a challenge and potential for future improvement. However, situation in this field is challenging and we will need to balance between expert recommendation regarding the useful indicators and reduction of number of indicators in order avoid administrative burden of GPs. Previous projects recognised a set of process and outcomes measures that need to be monitored at the individual patient level [14-16] and then might be aggregated across the patient samples of health plans, physicians, or other units. For several measures, including A1C, LDL cholesterol, and microalbuminuria testing, in some studies proportions are approaching 90% but other indicators like alcohol intake, end stage renal disease or laser treatment seem to have low validity and low feasibility [16, 17]. Organizational and systemic factors, in addition to physician factors, significantly affect physician performance and it needs to be supported within a broader environmental conceptual framework [18] that this study and implementation of observed results might support through individual and system models.

Throughout the entire project QCR tool was very useful guide. In the beginning, it gave the structure to the project, which was a backbone for conducting the pilot.

During the project, QCR tool was used to handle the communication with large number of partners. Thanks to it we have managed to coordinate a group work having constantly in mind our final goal - raising awareness about importance of regular and good quality diabetes monitoring both among GPs and patients.

CONCLUSIONS

The results have shown that checklists usage among general practitioners increased after intervention, and that education of general practitioners may contribute to better monitoring of patients with diabetes. According to previously reported data we can anticipate changes in chosen diabetes quality indicators as well [7], but we could not observe full extent of changes during the study since the time lag between education and collection of post interventional data was too short due to project duration and all planned activities. Qualitative research confirmed that most of general practitioners have positive attitude towards checklists, which can serve as reminders in regular monitoring of patients with diabetes. There were many possibilities for improving checklists and quality of care and our future recommendations for diabetes care improvement will be based on them.

This project was planned and prepared with the help of QCR tool, which had proven to be a feasible and practical framework for the designing and implementing our pilot.

Author's contribution

All Authors participated in study design and drafted

the manuscript; MS and TP performed field work and statistical and qualitative analysis. All the authors confirmed final version of manuscript for submission.

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Ethical approval

The ethical committee of Croatian Institute of Public Health approved the study.

Informed consent

Informed consent was obtained from all the participants included in the intensive group of the study.

Conflict of interest statement

None of the Authors declares competing financial interests.

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Culturally sensitive lifestyle intervention to prevent type 2 diabetes among Somalis in Finland: a pilot study using JA CHRODIS Recommendations and Criteria

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Abstract

Introduction. Somalis, particularly women, have high risk for type 2 diabetes (T2D). We designed and piloted a culturally tailored lifestyle intervention model to prevent T2D among Somalis.

Methods. The pilot was designed using the JA CHRODIS Recommendations and Criteria, with special emphasis on target group empowerment. Intervention consisting of risk identification and group and digital lifestyle counselling was created based on the existing Stop Diabetes-model. The 12-week intervention was conducted in the mosque.

Results. Of those at T2D risk, 24 participants (73%) agreed to participate in the lifestyle counselling. Mean participation rate in the group sessions was 50% and 76% of the participants used the mobile application. A statistically significant increase in vegetable intake was seen after the intervention. A non-significant increasing tendency was seen in all parameters of physical activity. All respondents considered counselling meetings very useful or useful.

Discussion. The piloted model proved to be feasible in providing prevention interventions to an underserved population group. Key success factor was active involvement of the target community.

Key words

- type 2 diabetes
- prevention
- lifestyle intervention
- immigrants

INTRODUCTION

The number of people with diabetes has increased steadily during the last decades all over the world. Lifestyle factors, such as obesity, an unbalanced diet, and low physical activity, are known to predispose to type 2 diabetes [1]. In addition, other broader environmental, socio-economic and cultural factors can impact people's risk of getting diseases, their ability to prevent them, or their access to effective lifestyle interventions and treatments [2, 3].

Due to climate change and international crises, the size and composition of most European populations are nowadays to a large extent determined by international immigration [4]. Also in Finland, the share of people with foreign backgrounds has grown rapidly during

recent years, the Somali population being one of the largest ethnic minority groups [5]. These changes in the population structure have an impact on the population health and need to be taken into account in health promotion and disease prevention.

Available data suggest that migrants tend to be more vulnerable to certain communicable diseases, injuries, poor mental health, and maternal and child health problems compared with the general populations in European countries [6]. It is well-documented that certain ethnic minorities have a higher prevalence of diabetes than non-minorities [7]. The study of Laatikainen et al. indicated that the prevalence of chronic diseases differs between ethnic groups also in Finland, and Somali population had significantly higher levels of diabetes

compared to any of the other migrant groups and native Finns [8]. These observed differences in the prevalence of chronic diseases between ethnic groups can be partly explained by differences in lifestyle-related risk factors. Previous studies have confirmed that obesity, physical activity, and unhealthy diet are more common among Somalis, and especially among women, compared with other ethnic groups and native populations [8-13].

Lifestyle interventions targeting people at risk have been shown to effectively prevent or at least postpone type 2 diabetes in various ethnic groups in several countries [14-17]. However, the applied interventions have usually been tailored to suit the needs of the majority, and hence their methods and results cannot be directly generalized to minorities. Moreover, the effectiveness of interventions in different immigrant groups is not well known, as people with immigrant background have been underrepresented in prevention interventions. Cultural factors may have a significant effect on whether an intervention done in other groups will be feasible for ethnic minorities [18]. Furthermore, people with immigrant backgrounds are a hard-to-reach population segment and may face a language barrier effectively preventing their participation in the interventions [18, 19]. In fact, people coming from other cultural backgrounds may not even perceive chronic disease prevention to be a part of health care and they may be less likely to seek preventive health services [20].

The review by Lirussi [18] concluded that many health-care systems are inadequately equipped to improve diabetes prevention and disease outcomes in ethnic minority groups. Better outcomes in diabetes prevention and care were shown to be achieved when the intervention programmes took place in the community settings, were culturally adapted and group-based, were delivered by a multidisciplinary group of health professionals, and aimed at improving self-management skills, self-efficacy, or self-empowerment [18]. However, most of the interventions in the review focused on improving glycaemic control among people with diabetes [18], and interventions focusing on the prevention of type 2 diabetes by lifestyle changes were scarce [19, 21].

In Finland, there are no existing public health interventions targeting specifically the needs of immigrant population groups. To address this gap, we created and piloted, in close collaboration with the local Somali community, a culturally acceptable prevention intervention, with the aim to improve risk identification among and participation of the Somali population. The existing StopDiabetes (StopDia) prevention intervention model was used as the basis and JA CHRODIS Recommendations and Criteria (QCR) as the framework to guide the development and implementation of the pilot action plan [22, 23]. This paper reports the experiences and results of the pilot action to improve lifestyle and prevent type 2 diabetes among Somalis in Finland.

METHODS

The use of QCR [22] in the pilot action planning has been described in detail in the guide for the implementation of JA CHRODIS Recommendations and criteria [23]. QCR consists of a set of nine Recommendations

and Criteria to improve prevention and high-quality care for people with chronic diseases: Design the practice, Promote the empowerment of the target population, Define an evaluation and monitoring plan, Comprehensiveness of the practice, Include education and training, Ethical considerations, Governance approach, Interaction with regular and relevant systems, and Sustainability and scalability [22, 23].

In this study, QCR was used as the framework to direct and monitor the implementation of the planned activities. The specifically addressed criteria were Practice design, Target population empowerment, Education and training, and Ethical considerations. The pilot was based on StopDia model, which is a Finnish type 2 diabetes risk identification and prevention model, created as part of the national StopDia project [24].

Cultural adjustment of an available intervention model

To ensure the suitability of the intervention model and tools, we set up a local implementation working group, including representatives from the participating research institutes and the Somali community in the capital region of Finland. Several workshops and group discussions were conducted, in order to map out the experiences and wishes of the Somali community in terms of the intervention and its execution. For the pilot, all questionnaires, forms, and materials including consents, study information letter, the diabetes risk test FINDRISC [25], group session materials, and the BitHabit application were translated to Somali language by the researcher with Somali background (IH) with help from volunteers from the Somali community. Group session materials and the BitHabit application contents were also culturally adjusted to be suitable for Somali population. For example, the traditional Somali diet was taken into account, and some prohibited foods, such as pork and alcohol, were excluded from the content of the intervention materials. For cultural acceptability, the interventions were organized in the mosque facilities, separately for men and women, and held in Somali language.

Recruitments of participants

The recruitment of participants was done in autumn 2018. The researcher with a Somali background (IH) organized several recruitment sessions in the mosque personally to give information on the pilot, thus increasing awareness and creating trust in the intervention. Personal contacts (word-of-mouth) and a written notification on public display aided the recruitment process, as well as the support and endorsement of the leader of the mosque, Imam. The participants recruited were Somali individuals living in the capital region in Finland, who had an increased risk to acquire type 2 diabetes. The risk was determined prior to recruitment by filling out the diabetes risk test FINDRISC. The FINDRISC is a validated method to identify, with 8 questions, an individual's likelihood to develop T2D within 10 years [25]. Additionally, women with children were enquired whether they had been diagnosed with gestational diabetes during pregnancy. The individuals who had in-

creased diabetes risk (12 points or more on the FIN-DRISC or previous gestational diabetes) were asked to join the study and received an informational handout regarding the pilot study. Three participants who got points lower than the predefined threshold (10 or 11) but were enthusiastic towards the intervention were also accepted. All participants filled out a consent form after the study procedure was explained to them verbally. Two groups were formed, one for males and the other for females. Originally, the aim was to have also a group with mobile application intervention only for those not willing or able to take part in the group sessions, but during the recruitment, it became apparent that all potential participants opted for group intervention combined with the use of the application. Participation was voluntary and the withdrawal was possible at any time during the intervention. The pilot action was conducted in accordance with the Declaration of Helsinki and the protocol was approved by the ethical committee of the Helsinki University Hospital.

Lifestyle counselling

The StopDia lifestyle counselling [24] comprised of group meetings (six meetings in 12 weeks) and the BitHabit healthy lifestyle support mobile application. The group meetings were organized in the mosque facilities, and the timing of the sessions was agreed within the groups, in order to maximise the possibilities of participation. The sessions were delivered in participants' own language, by the researcher with Somali background and Somali volunteer health care students. The group counselling was based on self-determination and self-regulation theories. Each group meeting lasted for approximately 1.5 hours, and each meeting had a similar structure and specific theme. The themes of the meetings were "Introduction to program and group", "Building daily rhythm", "Eating well and healthy", "Enjoying physical activity", "Bringing more activity into daily life", and "Being capable and successful" (Table

1). The meetings consisted mostly of group and pair discussions with the instructor more as a coach rather than a lecturer. Between the group meetings, the participants could, if they wanted, do homework and exercises using the participant's workbook, such as keeping a diary of their physical activities or fruit and vegetable consumption. The aim of the homework was to enhance the adoption of behaviours that were discussed during the face-to-face meetings.

The BitHabit healthy lifestyle support application was implemented as a mobile-optimized web application. The main functionalities of the BitHabit application were 1) browsing behavioural suggestions and selecting those that the users want to perform, 2) daily self-monitoring of the selected behaviours, and 3) getting summary feedback for habit formation in each of the 13 lifestyle categories. The application also provided information on other users' selections in an anonymous format through pop-up messages. Automated reminders were sent by emails and SMS messages if the user did not select any habits, add any performance, start using the application within two days after the first uptake message, or use the application for seven days. The application also had an additional self-learning section that provided reliable information on the prevention of type 2 diabetes [26]. The participants were instructed on how to use the application at the first group visit and could use the BitHabit throughout the 12-weeks counselling period.

Evaluation data collection

The impact of the intervention was assessed with clinical and lifestyle measures taken before and after the lifestyle counselling period, measuring participation and the use of the mobile application, as well as participants' experiences and opinions of the pilot intervention. Health measurement data included height (without shoes), weight (in light indoor clothing), waist circumference (on top of undergarments), and

Table 1
Lifestyle counselling among Somali population in Finland: content of group sessions

	Theme	Aim
Session 1	Introduction to program and group	Get familiar with other participants and the program Information on type 2 diabetes and lifestyle factors in its prevention
Session 2	Building daily rhythm	Observation of the daily rhythms of eating habits, physical activity, sedentary behavior, stress, sleeping, and rest Tools for management of daily life Goal setting and planning: Actionable behavioral goals to improve rhythm of daily life
Session 3	Eating well and healthy	Self-monitoring and reflection of dietary habits Principles of a healthy diet Goal setting and planning: Actionable behavioral goals for diet
Session 4	Enjoying physical activity	Self-monitoring and reflection of physical activity Principles of sufficient physical activity Goal setting and planning: Actionable behavioral goals for physical activity
Session 5	Bringing more activity into daily life	How can I nudge myself to healthy lifestyle? Goal setting and planning: Actionable behavioral goals for re-designing home environment to support healthy choices
Session 6	Being capable and successful	Self-evaluating program outcomes Learning and insights for future Planning for maintenance of behavior changes

Lifestyle interventions was based on StopDia prevention intervention model [24].

blood pressure. Weight was measured with electronic scale (SECA 877), height with a portable stadiometer (SECA 213), waist circumference (WC) with a measuring tape (Hoechst mass easy-check 53106) and blood pressure with an electronic monitor (OMRON M6AC). BMI was calculated as measured body weight (kg) divided by square of measured height (m²) for all participants. Health questionnaire data included background information and questions about participants' nutrition (a short and culturally adjusted version of a validated food frequency questionnaire [27]), exercise habits, and self-evaluation of the capability of making healthy lifestyle changes. In addition, participants were given the possibility to use an accelerometer to record their steps for a six-day period before starting the group meetings and after them. The evaluation measurements were completed by the trained volunteer health care or medical students who were also members of the Somali community. If requested, the measurements were completed by a measurer of the same sex as the participant. The web application collected a log of application usage, consisting of time stamped log of page visits as well as habit selections and performances.

Classification of variables

Education was categorized into three levels: higher education (college, academic degree), lower education (elementary school, vocational school, high school), and being illiterate. Perceived capability to make changes in diet or in physical activity was assessed with a four category questions. The information on capability was dichotomized by dividing people into "capable" and "not capable". Those who chose options "I am capable" or "I am very capable" were defined as capable of making lifestyle changes and all other categories were "not capable".

Vegetable consumption was inquired with a six category question and the variable was dichotomized as "eat vegetables daily" or "eat vegetables less than daily". Same categories were used for fruit and berries consumption. Eating breakfast, lunch or dinner was assessed with four category questions, and analysis was done using two categories: "3 times per week or more" and "2 times per week or less".

Statistical analysis

The data was analysed using SPSS (version 25). Usage log data were analysed using Matlab 2017b. For continuous variables (health measurements, steps), the values are presented as means and standard deviation at baseline and at follow-up, and further analysed with t-test. The categorical diet and physical activity outcomes are reported as number and percentage of participants belonging to each category and compared between baseline and follow-up to detect the possible effect of the intervention. BitHabit selections and performances are reported as medians and interquartile range.

RESULTS

About 90 persons of those who visited the mosque during the recruitment sessions (estimate based on FINDRISC form consumption) filled in the FINDRISC form. Altogether 33 persons (approximately 37%) were found at increased risk of type 2 diabetes. Of them, 24 participants (18 women and 6 men, 73% of those at increased risk) signed the informed consent and had their baseline measurements taken, 22 took part in at least one group session and 21 were measured at the follow-up. The mean age of women and men was 47.1 ± 10.1 and 43.6 ± 9.2 years, respectively (Table 2). The mean number of years the participants

Table 2
Baseline characteristics of the study population

	All n = 24	Women n = 18 (75%)	Men n = 6 (25%)
Age (years) (mean \pm SD)	46.2 \pm 9.8	47.1 \pm 10.1	43.6 \pm 9.2
Years in Finland (mean \pm SD)	22.3 \pm 6.6	23.3 \pm 4.8	19.5 \pm 10.2
Household size (mean \pm SD)	6 \pm 3	6 \pm 3	7 \pm 3
Marital status, n (%)			
Married	17 (71)	12 (67)	5 (83)
Single	3 (13)	2 (11)	1 (17)
Divorced or widowed	4 (16.7)	4 (22)	-
Education, n (%)			
Higher education	7 (30)	4 (22)	3 (60)
Lower education	14 (61)	12 (67)	2 (40)
Illiterate	2 (9)	2 (11)	-
Employment, n (%)			
Full- or part-time	8 (33)	4 (22)	4 (67)
Unemployed	3 (12)	2 (11)	1 (17)
Student	8 (33)	7 (39)	1 (17)
Stay-at-home mother	4 (17)	4 (22)	-
Other	1 (4)	1 (6)	-
FINDRISC (mean \pm SD)	14 \pm 2	14 \pm 2	12 \pm 2

Lower education: elementary, vocational or high school or lower; higher education: college or academic degree.

Table 3
Lifestyle counselling among Somali population in Finland: Participation in group sessions

	All (total n = 22)		Women (total n = 16)		Men (total n = 6)	
	n	%	n	%	n	%
Session 1	17	77	13	81	4	67
Session 2	11	50	8	50	3	50
Session 3	7	32	4	25	3	50
Session 4	4	18	4	25	0	0
Session 5	10	46	8	50	2	33
Session 6	18	82	12	75	6	100

had spent in Finland was 22.3 ± 6.6 years. Of the participants, 30% had high educational attainment (college or academic); on the other hand, 2 of the participants identified as illiterate. The mean household size was 6 ± 3 persons.

The mean participation rate in the group sessions was 50% (Table 3). The first and last sessions were the most popular, and the session 4 ("Enjoying physical activity") had the lowest attendance. After the 12-week lifestyle counselling period (Table 4), 80% of all the participants reported eating vegetables at least once a day. The same number for baseline was 50%. This change was statistically significant ($p < 0.05$). A non-significant increasing tendency was seen in all parameters of physical activity. No statistically significant changes were evident in clinical parameters; however, non-significant tendency

for reduction in waist circumference and systolic blood pressure was observed among all participants. At the follow-up, 91% of all participants reported feeling confident about their capacity to increase their physical activity, while at the baseline, the proportion was 61%. On the other hand, a reduction from 76% to 57% was observed in the perceived capacity to make dietary changes among all participants, but also this change did not reach statistical significance.

All participants who took part in group session were registered as BitHabit web app users. User activity varied greatly, but all users were actively viewing the habit selection window, even it did not lead to any selection of actions. Based on the application data, 19 (76%) users chose at least one habit and 17 (68%) marked at least one habit performance. The median and interquartile range for selected and performed actions were 12 (3.50-72.0) and 44.0 (17.8-431), respectively. The top 5 selections were physical activity, vegetables, grains, fat and oils, and sleep among women and men.

After the counselling period, we asked the participants to fill in a self-evaluation form concerning group meetings and their experiences of the pilot. Totally 20 participants filled in the evaluation form and all of them considered counselling meetings very useful or useful. All 20 participants would also recommend the intervention to others. Of the respondents, 16 (80%) evaluated that the topics of group meetings were interesting and relevant to them, and presented in a way that was easily understandable. They also considered that the home assignments were useful and that they received a proper amount of material to support them.

Table 4
Baseline (BL) and follow-up (FU) values in clinical and lifestyle-related factors

	All		Women		Men	
	BL (n = 24)	FU (n = 21)	BL (n = 18)	FU (n = 15)	BL (n = 6)	FU (n = 6)
Anthropometrics (mean \pm SD)						
Weight, (kg)	91.1 \pm 12.8	91.2 \pm 13.3	89.6 \pm 13.9	89.5 \pm 14.8	95.6 \pm 7.4	95.6 \pm 7.9
BMI, (kg/m ²)	32.8 \pm 4.3	32.9 \pm 4.4	33.9 \pm 4.1	34.1 \pm 4.3	30.0 \pm 1.4	29.9 \pm 3.5
WC, (cm)	106.2 \pm 9.4	105.5 \pm 11.3	104.6 \pm 9.2	103.7 \pm 11.9	111.1 \pm 9.1	109.9 \pm 9.3
SBP, (mmHg)	119 \pm 18	117 \pm 15	116 \pm 18	110 \pm 10	129 \pm 11	134 \pm 13
DBP, (mmHg)	78 \pm 9	79 \pm 8	77 \pm 9	75 \pm 6	81 \pm 8	86 \pm 9
Diet (%)						
Capable to make changes in diet	76	57	69	53	100	67
Vegetables daily	50	80*	50	73	50	100
Fruit and berries daily	52	52	53	47	50	67
Breakfast three times or more per week	91	95	88	100	100	83
Physical activity (%)						
Capable to increase physical activity	77	91	75	93	83	83
Incidental exercise three or more times per week	48	86	51	80	40	-
Planned exercise three or more times per week	23	48	13	40	60	67
Steps per day (mean \pm SD)	3771 \pm 2866	4568 \pm 2080	2278 \pm 1692	3962 \pm 1471	6757 \pm 2360	5377 \pm 2616

WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure.
* $p = 0.016$

In the self-evaluation form, more than half of those who filled it in reported having made some changes in their daily lifestyle habits. Out of 20 respondents, 70% (n = 14) reported having increased their vegetable consumption, 50% (n = 10) reported eating less sugary snacks and sweets, 45% (n = 9) increased amounts of whole grains in their diet, and 55% (n = 11) reported more frequent meal patterns and increased amount of exercise. Other reported activities were: taking stairs instead of an elevator and paying more attention to sleep rhythm. Also, BitHabit app was found to be either “very useful” or “useful”. Altogether 12 (60%) respondents evaluated that they were “very likely” to continue making healthy life style changes in the future, and all the rest (40%) evaluated that they were “likely” to do the same. Data on participants’ perspectives on the intervention suggest that they were very satisfied with the concept and content of the intervention model.

DISCUSSION

Given the higher prevalence of diabetes in certain ethnic minorities, there is an urgent need to develop culturally specific practices to prevent type 2 diabetes. In this paper, we describe the process of cultural adjustment and implementation of an available intervention model and report the experiences and results of the pilot action to prevent type 2 diabetes among Somalis in Finland. In general, the co-created intervention model consisting of risk identification and lifestyle counselling was feasible and well-received by the target community, and suggestion towards modest improvement in lifestyle was observed during the 12-week counselling period. Furthermore, out of 22 respondents, a total of 20 evaluated that they were likely to continue with the lifestyle changes after the counselling period.

Migrants have their own knowledge and attitudes about health issues which influence their health-seeking behaviours, approaches to disease prevention, and decision-making in regard to acting on the guidelines of health care providers [28]. Previously, it has been shown that the use of group counselling and making cultural adaptations to the interventions together with the target community members could result in better outcomes in the prevention and care of type 2 diabetes among immigrant populations [18]. Also, in our pilot, taking the culturally and linguistically adjusted group-based intervention close to the participants, and having it delivered by experts who themselves belong to the target community, proved to be a feasible concept of providing preventive intervention to this under-served population segment.

Regular physical activity and diet are key components of lifestyle intervention in people with high risk for type 2 diabetes [15, 16]. However, studies addressing these issues in ethnic minorities, especially within Somali population, are scarce. In Europe, culturally adapted lifestyle interventions have mainly been carried out in South Asian immigrants with high risk for diabetes [19, 21, 29, 30]. These preventive intervention trials have suggested more modest effects in South Asian adults than in European-origin adults. However, in a recent meta-analysis lifestyle interventions in South Asian

populations resulted in a clinically important 35% relative reduction in diabetes incidence, despite the modest changes in lifestyle related factors [31]. In the present pilot, the observed changes in behaviours and known risk factors of type 2 diabetes were moderate in African immigrants, but these small changes in important behaviours (e.g. increase in consumption of vegetables) could have a large impact in diabetes risk reduction in long-term and on population level, like previously was shown among Asian immigrants [31].

Interestingly, participants’ self-efficacy in making lifestyle changes seemed to shift in a somewhat unexpected way. After the counselling period, the participants reported increased perceived capability to make changes in their physical activity behaviours, while their perceived capability to improve their diet seemed to decrease. The reason for this might be that “healthy diet” as a concept is multi-dimensional and therefore probably more difficult to grasp during a relatively short time than the rather simpler message to increase all physical activity by, for example, walking more. The “recommended diet” might also be in conflict with one’s own perception of a proper, traditional diet and therefore more difficult to adopt.

The qualitative study of Gele *et al.* explored the experiences of Somali immigrant women in the reception of preventive health services in relation to type 2 diabetes in Norway [32]. Somali women were found to have a good knowledge of diabetes and its risk factors. However, participants reported unhealthy lifestyle habits, such as sedentary lifestyle and unhealthy diet, and this was partly explained by poor access to tailored health information and tailored physical activity services [32]. Further, the numerous U.S. studies have documented the disparities in the usage of preventive health services between immigrant populations [33, 34], and the disparities have found to be greater for Somali patients compared with non-Somali patients [34]. In our pilot, we showcased how providing the risk screening and lifestyle counselling services in facilities that people know and where they feel secure, by trustworthy people from their own community, abolishes the barriers against preventive interventions identified in the research literature.

In general, participants were very satisfied with the conduct and content of the intervention and they expressed interest to continue the lifestyle changes also after the pilot period. However, some challenges were faced during the implementation which offered us several important learnings to be considered for future prevention activities in Somalis and other immigrant groups. The recruitment of men was more difficult than anticipated. The most important reason was that the men’s risk factor levels, especially BMI, tended to be lower as compared to women, which is confirmed also by literature [35]. In the future chronic disease prevention activities, the inclusion criteria should be extended to cover other risk factors, such as smoking, that are more prevalent among men [36].

Furthermore, some participants had difficulties in attending the scheduled counselling sessions due to lack of time or conflicting timetables even though the group

sessions' timetable was agreed together. One reason for this was that the participants had larger families than the general Finnish population [37], thus arranging child care during the group sessions could be pivotal for enabling participation of especially the mothers. This, in turn, might actually increase the impact of the whole intervention, as the mothers are usually in charge of the dietary choices within the family.

Originally, we aimed to offer a digital-only intervention for those individuals with increased risk, but with no time or interest to take part in the group meetings. However, during recruitment it became evident that the digital-only intervention was not appealing to this target group and all participants wanted to sign up for the group intervention. It has been suggested that lack of digital skills might be a barrier against participation of some population groups in state-of-the-art interventions that are (partly or solely) conducted digitally [38]. This, however, proved to be no issue in this pilot group, as all participants did register as BitHabit users and 76% chose at least one healthy habit to pursue. Nevertheless, there may be other cultural factors at stake. Previously, the use of culturally competent facilitator has been shown to be one of the explaining factors for successful health promotion approaches among immigrant women [39]. Also, in the study of Gele et al, most Somali-origin respondents preferred preventive health information in their own language and through oral communication combined with visual materials [32]. These findings emphasise the importance of using an instructor with adequate cultural competence, not only digital tools, when implementing preventive interventions among immigrant groups.

The used strategies of the empowerment-based intervention, such as providing culturally adapted intervention materials and open communication with target group, were the main strengths of our intervention. Also, the evidence- and theory-based intervention model, activities which took place in a facility that was familiar and convenient for the participants, culturally competent facilitator, inclusion of the target group members into planning and implementation of the intervention, and holistic approach to healthy lifestyles were other strength of this pilot. Moreover, the QCR provided a feasible and practical framework for the designing and implementing this pilot [22, 23]. It steered focus on the whole picture at the beginning of the project and forced to ponder the practical details in advance. However, there was a weakness in terms of scientific evaluation, because due to low sample size in this "feasibility pilot" the observed quantitative results could be evident but

not statistically significant, and there was no control group for comparison. However, due to the nature of the study, just by their participation, valuable knowledge on this population was gained.

In conclusion, the piloted model proved to be feasible in providing prevention interventions to an underserved population group. The co-created T2D prevention intervention model could be transferred to other Somali communities in Finland and other countries, but would require close collaboration with the target population as well as training of the local implementers. Same intervention could be feasible, after adjustment and translation, for other immigrant groups and would benefit people with other risk factors also, not just those who are at high T2D risk. In the future, it would be important to establish collaboration between health care services and preventive intervention providers. If the model will be implemented on a large scale, it could have an important effect also as regards to health disparities between population groups.

Author's contribution

JL, KW, IH and EV planned the study design. EV carried out the statistical analyses. KW drafted the manuscript. IH, JL, EM and ML contributed to a critical revision of the work. All the authors read and approved the final version of manuscript. KW takes authors responsibility for the contents of the article.

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Conflict of interest statements

None

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Redesigning diabetes care delivery in Serbia, using JA CHRODIS Recommendations and criteria

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Abstract

Introduction. Managing non-communicable diseases (NCDs) requires redesigning health care delivery to achieve better coordination of services at all levels of health care. The aim of this study was improving prevention and strengthening high quality of care for NCDs by using type 2 diabetes as a model disease.

Methods. The mix method approach served to analyse the impact of the intervention processes. Source of information were routine health statistics, interviews and observation. Key Performance Indicators in defined Improvement Areas assisted in the quality of diabetes care assessment.

Results and discussion. During the study the National Diabetes Centre (NDC) was established. The NDC experts organized numerous educational events, 316 physicians and nurses have participated. New electronic data base was implemented in 20 pilot Primary Health Care Centres (PHCCs) with 38,833 electronic diabetes records.

Conclusions. The intervention led to establishment of the NDC, strengthening competences of health care professionals and to the renewal of the Diabetes Care Units in PHCCs included in the study.

Key words

- type 2 diabetes
- National Diabetes Centre
- Primary Health Care Centres
- electronic diabetes records

INTRODUCTION

Non-communicable diseases (NCDs) present the major burden of morbidity and mortality in Serbia. In 2017, the diabetes was the 7th leading cause of death and 4th leading cause of burden of disease measured by DALYs per 100,000 population [1]. According to National Health Survey from 2013, 7.6% of adult population had been diagnosed with diabetes, while estimates in 2018 are presenting 600,000 people living with diabetes (8.1% of total population) [2, 3]. However, it is estimated that 36% of individuals with type 2 diabetes (T2D) are not diagnosed to have a disease. Almost half of the people with diabetes are at working age and approximately one third already have one or more late complications by the time of diagnosis. This is why the diabetes presents a large economic burden on individuals, their families and national health care system in Serbia.

Today, based on the new Health Care Law, the health care system in Serbia is centrally managed and vertically

structured [4]. The 2019 Health Care Law and 2019 Health Insurance Law foster the concept of the “chosen doctor”, which was established by the 2005 Health Care Law to promote a culture of continuous quality improvement at all levels of health care. The health care system is improving information for patients on their rights and their roles in decision-making processes. Patient choice is linked to the concept of the “chosen doctor” in primary care, who acts as a gatekeeper to other levels of care. Until 2005, significant role in diabetes care had Diabetes Care Units (DCU) in Primary Health Care Centres (PHCCs). However, the Law on Health Care in 2005, changed the structure of diabetes care [5]. The majority of diabetes care units were cancelled, which had the negative influence on the quality of diabetes care and contributed to the overload of services on secondary and tertiary level. The new incentive was the National Programme for Early Detection and Prevention of Type 2 Diabetes at the Primary Health Care in Serbia adopted

in 2009 [6]. This programme is guiding continuous quality improvement of diabetes care at primary health care level up to today. Although, Serbia developed modern electronic health record on primary health care level, there is a lack of specific data on patients with diabetes for monitoring the burden of diabetes and boosting the quality of diabetes care. Altogether, this emphasizes the importance of comprehensive implementation and further upgrading of preventive measures, early detection of diabetes and improvement of diabetes health care and quality of life of people with diabetes, as well as other non-communicable diseases.

In that context, the aim of the study was improving prevention and strengthening high quality of care for NCDs by using T2D as a model disease.

The study was based on the National Program for Prevention and Early detection of T2D and involves relevant stakeholders in the area (Ministry of Health, Republic Institute of Public Health of Serbia, Medical Faculty, and Clinical Centre of Serbia). The project has used the Quality Criteria and Recommendation Tool (QCR Tool) aimed to reintroduce the practice recognized as efficient both among patients and health professionals [7, 8]. The use of QCR tool enabled the implementers to assess the intervention and to identify its strengths and weaknesses, and also to adjust the action plan accordingly.

METHODS

Intervention(s) and population

Based on the scope of the study, and starting from the Quality Criteria and Recommendation Tool (QCR Tool), Strengths-Weaknesses-Opportunities-Threads (SWOT) analysis was performed to identify possible strategic options after cross-cutting of strengths/weaknesses and opportunities/ threads. The QCR were adopted and implemented as described below.

Practice design

The action plan defined the aims, objectives and methods of the study clearly. The data on the prevalence of T2D is drawn from the National Health Survey and the registry for the diabetes. Representatives of patient organization are included in the design of the action (PA). There is a need for more thorough assessment of the needs for employment of health care professionals in Primary Health Care Centres (PHCCs) who would be in charge of Diabetes Care Units (DCUs).

The intervention proposed is leading to earlier detection of T2D and better control of the disease. The indicators for monitoring are taken from the Rulebook on Indicators of Quality in Health Care and show the possibilities for the successful disease control.

Education and training

Educational elements are included in the practice to promote the empowerment of the target population – health personnel of DCUs.

Governance

The practice included organizational elements, identifying the necessary actions to remove legal, manage-

rial, and financial or skill barriers. The practice is based on the recommendations from the National Program for Prevention and Early Detection of Type 2 Diabetes. The contribution of the target population, carers and professionals was appropriately planned, supported and resourced. The action plan is created in collaboration with all the relevant stakeholders and the National Diabetes Centre NDC) as a reference institution monitors the implementation.

Serbia is in the process of implementation of the integrated health information system, which allows easier communication between the health care professional on the different levels of the health care. There was a defined policy to ensure acceptability of information technologies among users (professionals and target population) as Serbia has adopted the National Program for Prevention and Early Detection of Type 2 Diabetes.

Sustainability and scalability

All the relevant stakeholders show strong support for the sustainable implementation of the program. The program includes the work on the primary health care level which is easily accessible for patients, regular educations for health care professionals done by the experts and the formation of the NDC which would be the referral and the crown organization for the process. The implementers and the stakeholders support the broader implementation of the practice.

Several barriers were found during the implementation, which were gradually overcome. At the beginning of the implementation, the Local Implementation Working Group (LIWG) saw the absence of national coordination centre for overall management of diabetes care as the main barrier. Despite the existence of a national Registry for Diabetes, it could provide only data about mortality and morbidity related to diabetes, but not for the comprehensive monitoring of quality of diabetes care and its cost implications. In addition, DCUs at PHCCs had limited opportunities to provide quality care for diabetes type 2 patients, as the legislation foresaw the possibility to establish DCUs within a PHCC only if the catchment area sufficiently large (equal to one district). Due to the shortage of health care staff, workload in DCUs was high, and specific training on the utilisation of toolkit for prevention of T2D was missing.

However, important enablers supported implementation. The LIWG stirred stakeholder's support (particularly from the Ministry of Health). The willingness to improve the legislation regarding health care quality, to strengthen DCUs at the primary level by investing additional funds in continued education on diabetes care were important enablers. National guidelines for diabetes care with well-defined, evidence based practice design was in place. Also, the National Program for Prevention and Early Detection of Type 2 Diabetes supported the strengthening of primary health care activities during the implementation. The process of improvement of the national health information system already started. Within this, the introduction of the Book of Electronic Diabetes Record (BEDR), improved the possibilities for evaluation of the quality of diabetes care.

In Serbian action, target population were adults aged over 45 years with risk for diabetes and adult people with diabetes. The implementation working group defined five improvement areas (IA) and consequently five interventions:

- IA1: Establishment of NDC) at Clinic for Endocrinology Diabetes and Metabolic Diseases, Clinical Centre of Serbia;
- IA2: Innovative service delivery by reintroducing DCUs in PHCCs;
- IA3: Control of implementation of the National Program for Prevention and Early Detection of Type 2 Diabetes. The intervention plan is presented in the Figure 1;
- IA4: Intensifying capacity building of health staff through training and education of physicians and nurses, through the newly established NDC;
- IA5: Implementation of the health information technologies with the focus on the electronic registries of patients and high-risk individuals.

Members of the implementation working group started an intensive work on improving the electronic health record of patients with diabetes at the PHCC in order to establish the electronic Register of Patients and high risk individuals. In cooperation with the CEDMD, the Institute for Public Health has developed Manual for physicians at the PHCCs for the appropriate data entry in Registry.

Intervention aiming to implementation of the BEDR contains all functionalities necessary for the integration to existing electronic health record. The system allows user-friendly monitoring of T2D control, but also, supports education and self-control of patients. Physicians obtained a useful tool to identify a patient with bad diabetes control.

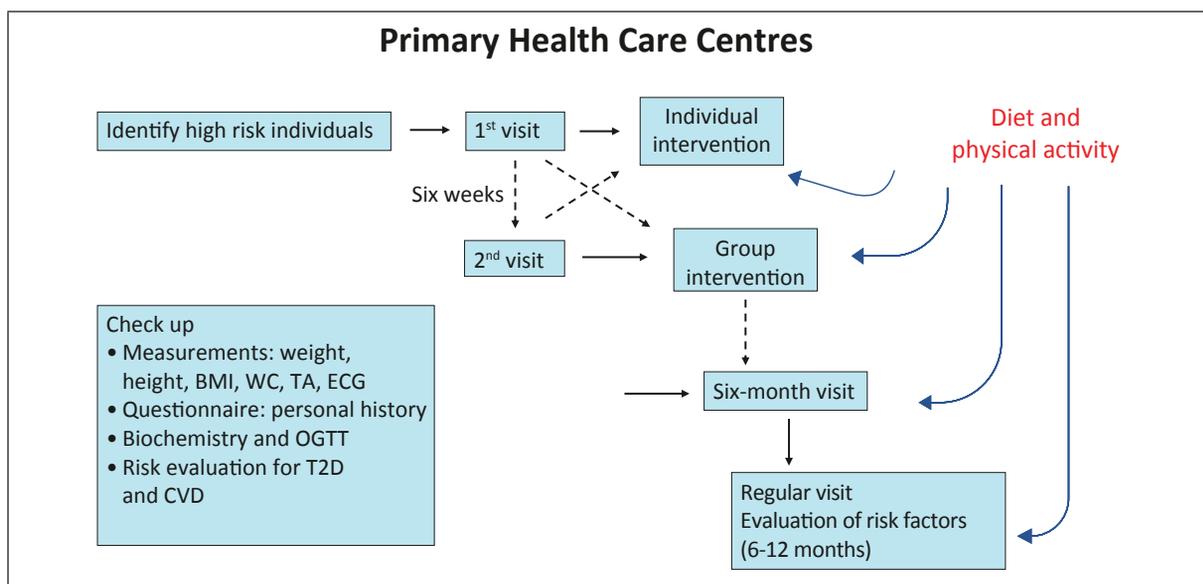
Study of the intervention(s)

In order to analyse the impact of the intervention processes, mixed methods approach (quantitative and qualitative) was used. Key performance indicators for evaluation activities in defined improvement areas of the action were:

- IA1: Report on establishment of NDC. List of indicators for quality of diabetes care. Report on indicators of quality of diabetes care during each year of implementation.
- IA2: Report on the number of detected high risk individuals for T2D during each year of the project period. Report on the number of patients with newly diagnosed T2D included in the health care system during each year of the project period. Report on the number of high risk individuals for T2D included in preventive intervention during each year of implementation, report on the effectiveness of the preventive treatment of high-risk patients for T2D during each year of implementation.
- IA3: Report on improvement of DCU. List of amendments for diabetes care legislation (National Plan for Development of Diabetes care).

Also, for the IA4 the number of trained staff served as a key indicator together with before-after evaluation of each training. The focus of study for the IA5 was success in implementation of the BEDRs assessed by achieved expectation of the health care staff, usability in self-control of patients with T2D and number of records entered in BEDR per PHCC.

To establish relations between the interventions performed, the results of the key indicators will be ready only at the end of 2019, and then they will be compared with the period before intervention. For the IA4 and IA5 comparison is not possible as the organized system



*BMI body mass index, WC waist circumference, TA blood pressure, ECG electrocardiography, OGTT oral glucose tolerance test, T2D type 2 diabetes, CVD cardiovascular disease.

Figure 1 Prevention of type 2 diabetes in Republic of Serbia Intervention plan.

of continuing education for better diabetes care and the system BEDR did not exist.

Measures

Processes and outcomes of the intervention were measured by selected Organization for Economic Cooperation and Development (OECD) indicators for process and proximal outcomes of diabetes care. These indicators are recommended by OECD international expert group for assessing the effectiveness of health care delivery on a global scale.

1. Process measures:
 - a. annual HbA1c testing: percentage of patients with one or more HbA1c tests annually;
 - b. annual eye exam: percentage of patients who received a dilated eye exam by an ophthalmologist during the current year.
2. Outcome measures:
 - c. HbA1c control: percentage of patients with most recent HbA1c level <7.0% during the measurement period of one year before the control (target value for the most individuals with diabetes).

All measures use the number of clinically diagnosed patients with diabetes as their denominator. These measures are routinely published by the Republic Institute of Public Health of Serbia, and there were no additional costs.

In 2020, the electronic system of the BEDRs will allow more possibilities for monitoring and new measures.

Study analysis

All actors in the public system are obliged to report regularly to the institutes of public health on their activities related to public health and health care services at primary, secondary and tertiary level. The Institute of Public Health of Serbia (IPH) Batut is responsible for the collection of data on population health, the work of health institutions (that is, classical indicators related to health services outpatient and inpatients visits, average length of stay in hospital, indicators of healthcare quality, cancer screening coverage, etc.), the analysis of collected health indicators, templates of measures to improve public health (for example, in health promotion: number of mass-media campaigns per regional IPH or health education interventions for prevention of the risky life styles). The system of health reporting serves the monitoring and analysis of the health status of the population, the planning and programming of health care, the monitoring and evaluation of the implementation of health care plans and programmes, statistical and scientific research and other needs.

Currently more than 200 health care institutions in the public sector, from a total of 355, have electronic health records (EHRs). Out of 158 PHCC, 152 have electronic information systems that are in use, as well as the electronic history of the disease in over 50 hospitals. All software is compliant with the national standard, the 2009 Rulebook on the Content of Technological and Functional Requirements for Establishing the Integrated Health Information System. This situation will serve

as an advantage to perform analysis of data within the BEDR.

For the purpose of this intervention analysis, the data are presented descriptively as the percentages of patients with HbA1c determined and of patients referred to ophthalmologist examination.

The support from the stakeholders was assessed through the number of face-to-face meetings with them. Regarding patients as the most important stakeholders, the national survey on patient satisfaction has been on-going annually since 2004 [9].

The local implementation team held series of face-to-face meetings with the relevant stakeholders in order to insure their support for the project and for further steps. Ministry of Health expressed long-term commitment to support newly established NDCs, together with provision of financial resources for continuing education of health personnel employed in DCUs. Patient organizations articulated readiness to involve more members with T2D, while professional staff appreciated working together with their T2D patients to develop the culture of patient-centred care.

The satisfaction of participants with educational meetings was assessed using the questionnaire on the satisfaction [9] with lectures, lecturers, topics, usefulness of the presented information, etc. Also, entrance and exit test of knowledge served for assessment of competences gained through training.

The program includes the work on the primary health care level which is easily accessible for patients, regular educations for health care professionals done by the experts, the formation of the NDC which would be the reference organization for the process of integrated care, while the book of electronic diabetes records makes improved monitoring of the diabetes care quality.

RESULTS

The intervention led to the establishment of the NDC as reference institution, which is the coordinating centre for Diabetes care and education in Serbia now. The NDC has its mission, vision, objectives, planned activities with performance indicators, responsible personnel, and sources and amounts of budgeting. In total, 39 health professionals are performing planned activities within this functional centre, out of which 14 physicians (specialist of internal medicine, and among them 10 subspecialists in endocrinology, 11 teaching staff – 6 professors, one associate professors, 4 teaching assistants) and 25 nurses. The NDC operates within the Clinic for Endocrinology, Diabetes and Metabolic Diseases of the Clinical Centre of Serbia. This institution is the International Diabetes Federation (IDF) Centre of excellence for education and patient care. Objectives of the NDC are education of health professionals in advancements of diabetes care, health technology assessment (HTA), patient care, counselling in application of different interventional tools such as motivational interview in changing behaviour by introducing healthier nutritional habits or regular physical activities. The experts from the NDC are conducting monthly educations for the health care staff from PHCC who are working with patients with diabetes.

During the study 316 health professionals attended training performed by NDC – two per each of 158 PHCC. The educations lead to improvement of diabetes care and the abilities of health professionals to embrace population based approach in improving health status and quality of life of patients with diabetes through regular, adequate treatment, and lifestyle interventions.

Prevention of T2D should be carried out in accordance with the recommendations of the National programme for prevention and early detection of T2D:

1. detection of high risk patients for T2D by a systematic approach;
2. detection of high risk patients for T2D by special approach;
3. determination of pre-diabetes diagnosis;
4. introduction of high-risk individuals for T2D in the registry;
5. prevention of T2D by population-based approach to society;
6. prevention of T2D by a population-based approach to an individual;
7. T2D prevention by special approach for people at high risk for T2D;
8. introduction of a patient with newly diagnosed T2D into the diagnostic and treatment system, as well as in the registry of patients with T2D within the PHC.

To identify adults at high risk for T2D we have been used Finnish Diabetes Risk Score (FINDRISC). It is a questionnaire that gives an estimate of risk for getting diabetes in the next 10 years. It serves as a “mini-intervention” as it gives information about diabetes risk factors in a simple and easy-to-understand way. If the score value is high (>15) a blood test is recommended to detect previously undiagnosed diabetes (OGTT being the “gold standard” test). Diabetes patients are further introduced into treatment system within the PHC, while the rest high risk individuals without diabetes undergo lifestyle intervention. Lifestyle modification is focused on healthy diet and physical activity.

The improvement and/or renewal of DCUs leads to easier access to proper diabetes care, which are easily accessible to patients and patients do not need specialists at secondary or tertiary services for routine treatment of diabetes. This intervention also leads to reduction of workload on secondary and tertiary levels, as

only patients in need for specialist care are referred to higher levels of health care.

The capacity building of health care professionals working in DCUs was done by trainings in the NDC which academic staff conducted monthly education and included total of 316 health care professionals as mentioned above, physicians and nurses who are working in PHCC. The lectures were held for teams consisted of physicians and nurses, but also there were separate educational workshops, different workshops for the doctors and nurses. All trainings included case studies of real life situations and demonstration of clinical skills with role playing. All health care professional who attended trainings expressed great satisfaction with the education, as the average score for all conducted workshops was 4.97/5. Total of 89.15% of the participants stated that they will use the knowledge acquired during the workshops in every day practice. The participants stated that the workshops were creative, useful and interactive and commended the organization of the education by the NDC.

Out of eight PHCC included in the study, the percentage of patients with diabetes who were referred to the ophthalmologists for funduscopy and the percentage of patients who have had their HbA1c level examined at least once per year rose in five PHCC. According to the latest data the highest percentage of patients referred to ophthalmologist was in PHCC Uzice. Unfortunately, in 2018, the percentages of patients referred to ophthalmologist varied depending on existence of ophthalmologists in the PHCC. As the year 2018 does not represent the best year to assess the results of the intervention (which started in the second half of 2018), data that will come in the first half of 2020 will be better to make analysis. The same is with the percentages of patients with HbA1c level determined annually in 2018. The highest rise in the percentage of patients with HbA1c levels determined was in PHCC Kragujevac which rose more than three times in 2018 comparing to the year before intervention (Table 1).

Besides development of the BEDR, the intervention was spread to additional 12 PHCCs, in total 20 PHCCs established BEDR. The motivation of staff to utilize the new system was remarkable, as only in two weeks, during 2019, 38,833 electronic records were

Table 1
Selected quality indicators retrieved from the BEDR system (based on 38,833 patients' records)

Quality indicators (%)	Zemun	Stari grad	Novi Sad	Kragujevac	Kruševac	Total
HbA1c >1	37	39	35	32	29	34
LDL-c >1	38	29	22	53	24	33
Screening rethinopathy	19	30	30	20	13	22
Screening nephropathy	14	10	20	11	10	13
Frequency of dialysis	1	0.3	1	0.2	0.5	0.6
Frequency of amputations	0.1	0.3	1	0.2	0.1	0.3

*The data are presented as percentages of patients with one or more HbA1c and LDL-c tests annually. Also, it was presented the percentages of patients screened for microvascular complication (retinopathy and neuropathy), and frequency of dialysis or amputations as indicators for macrovascular complications of diabetes in the PHCC.

formed by transferring data about patients with T2D from the paper records of PHCC (Figure 2).

Also, the BEDR allows direct improvement in monitoring of diabetes care with presentation of quality indicators on daily basis (Table 2), while full impact of the action will be visible only in 2021.

After implementation of the BEDR, before deployment in all PHCCs in Serbia, BEDR started with implementation in 12 more PHCCs.

DISCUSSION

The establishment of NDC creates the coordinating reference organization for the health care professionals working in DCUs in Serbia and enables better health care outcomes. In that context, by organization of continuous education it provides the support for physicians working at the primary and secondary health care level in a form of tertiary institution with experts in the field of diagnostics and treatment of diabetes.

The implementation of step-wise protocols for identification of patients in high risk for T2D and of patients with previously undiagnosed T2D leads to establishment of systematic approach to these patients.

The action plan was developed in accordance with National Program for Prevention and Early Detection of Type 2 Diabetes, National Guidelines for Diabetes Care and results of relevant international studies. Many randomized, controlled clinical trials have demonstrated a significant impact of lifestyle changes in prevention of T2D among high risk individuals [10-12]. Two most important interventions, Finnish Diabetes Prevention Study (DPS) and Diabetes Prevention Program (DPP) showed that people who were at high risk reduced their risk of developing diabetes by 58% over 3 years through lifestyle intervention [13, 14].

EU/IMAGE project, development of European guidelines for prevention of T2D and toolkit for the pre-

Table 2

Percentage of patients with diabetes who were referred to the ophthalmologists for fundoscopy and HbA1c level examined at least once yearly (2018) in PHCC

Primary health care centres (PHCC)	Ophthalmologists exam (%)	Measurement of HbA1c (%)
Palilula	24.5	52.12
Savski venac	40.13	37.22
Stari grad	20.55	33.97
Zemun	12.39	23.11
Uzice	94.5	94.5
Novi Sad	46.4	18.47
Kragujevac	8.7	61.85

*The data are presented as percentages of patients referred to ophthalmologist varied depending on existence of ophthalmologists in the PHCC. The same is with the percentages of patients with HbA1c level determined annually in 2018.

vention of T2D in Europe with practical guidance for the lifestyle intervention with the population based approach. Deliverables of this project are incorporated in our National Program for Early Detection and Prevention of Type 2 Diabetes [15, 16]. The implementation of higher quality health services for diabetes in primary health care practice in Serbia bears an enormous potential to save lives, respectively to decrease years lived with reduced quality of life and it may reduce clinical costs by as much as a quarter [17]. In addition, Serbian burden of disease study has shown that a preventive programme with a relatively small budget may achieve risk factor reductions resulting in about the same amount of quality adjusted life years saved, not only through the prevention of diabetes but also of other diseases [18].

The regular educations for physicians and nurses,

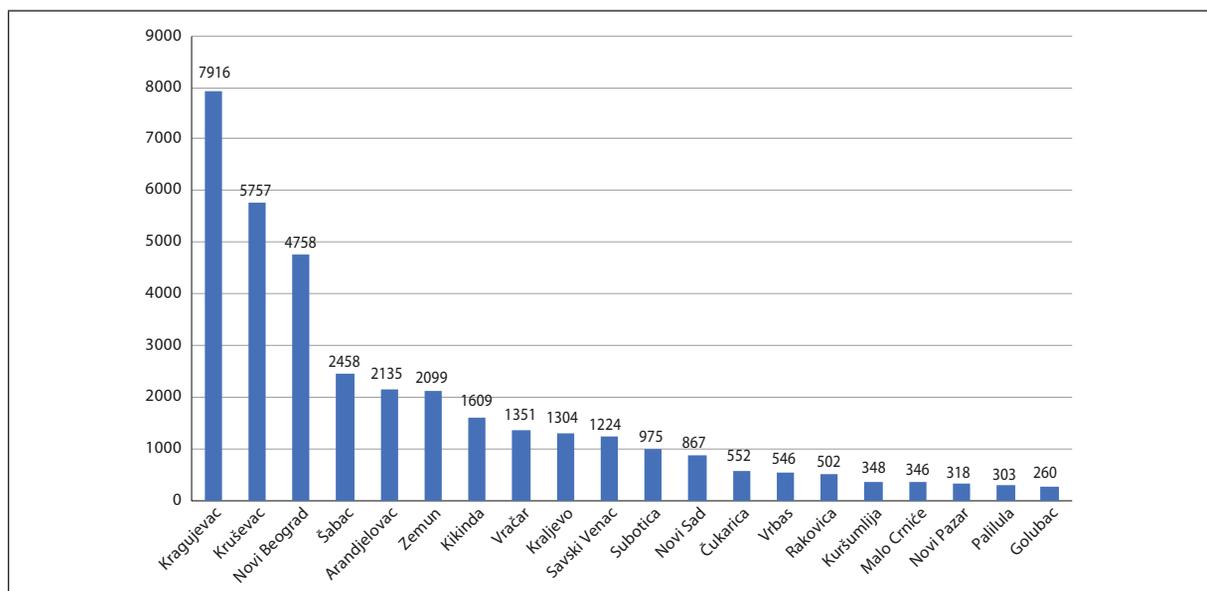


Figure 2

The number of established records per Primary Health Care Centres. Republic of Serbia.

which are organized in the NDC create opportunities for health care professionals who are working with patients with T2D to improve on their knowledge and every day practices, as well as to create the uniform approach to diabetes care in the entire country. Also, the regular educational events serve for upgrading of staff motivation and their satisfaction leading indirectly to better quality of diabetes care.

Established system of electronic diabetes records secures better monitoring and advancing in diabetes care quality.

The BEDR embraced the concept of the shared-care: quick access and information exchange, and better coordination of health care providers in the cycle of diabetes care. Also, the BEDR secures the platform for continuous quality improvement of diabetes care by allowing better monitoring of the health care quality at all levels with indicators for the process of the care, proximal and distant outcomes. The main expectations are the reduction in frequency of diabetes complications, decrease in the premature mortality among people living with diabetes and decline in costs of diabetes care.

Main results of MANAGE-CARE project demonstrated that managing chronic conditions such as diabetes, requires redesigning health care delivery to achieve better coordination of services, more integrated approach and integrated health care system across levels [19]. This project particularly emphasized empowerment of people living with T2D. While achieving improved diabetes management, according to preliminary results of Early prevention of diabetes microvascular complications in people with hyperglycaemia in Europe (ePREDICE) study, prevention and early detection of cardiovascular and other complications would have a huge impact in reducing morbidity and mortality of these chronic conditions [20]. Finally, JA CHRODIS results – Quality of Care Recommendations and SWOT analysis were recently applied, tested, adapted and implemented at the end of 2018 and throughout 2019 [7, 8].

CONCLUSION

In conclusion, Serbian intervention led to establishment of the NDC and organization of educations for health care professionals from all primary health care centres in Serbia. Furthermore, led to the renewal of the DCUs in PHCCs included. The DCUs are recognized by the patients with diabetes as the most accessible and friendly institution in the Serbian health care system. The health care professionals in the DCUs are well-informed about each patient who is regular in the DCU, and they establish the relationship full of mutual trust which ultimately leads shared decision making as the central feature for patient-physician relationship, and better health outcomes for these patients. The continuing education of the health care professionals from all primary health care centres will improve diabetes care in entire country.

The implementation of the step wise approach to identify patients with T2D and patients in high risk for development of T2D can lead to earlier diagnosis of T2D, regular physical activity and diet intervention,

timely introduction of therapeutics and prevention of the late complications of diabetes, which are highly prevalent among Serbian population.

It added to the previous practice by introduction of the NDC, and regular educations of health staff by the experts from the NDC. For the first time, Ministry of Health of the Republic of Serbia devoted direct budget resources for continuing education in T2D for primary health care professionals. The preventive intervention and lifestyle intervention can have positive consequences on population health as they reduce the likelihood of development of T2D. Nation-wide introduction of this practice will lead to reduction in incidence of T2D, in prevalence of late complications of T2D and in the improvement of quality of life of patients with diabetes.

The implementation of the BEDR system proves to be efficient in monitoring of diabetes care quality at primary health care level, and it is also appreciated by health care professionals in this phase.

The use of QCR tool enabled the implementers to assess the intervention and to identify its strengths and weaknesses, and also to adjust the action plan accordingly.

During the action, several key enablers were identified by following the QCR Tool in implementing better quality of health care for other diseases. Well-defined practice design supported by national guideline and programme of prevention was one of enablers, which also secures the comprehensiveness of the practice. To empower target population, the concept of the clear description of population (people under risk to develop certain disease) will serve for replicability of the QCR to prevention of other diseases. After full implementation of the BEDR, it became clear that similar electronic system, based on upgraded guidelines and programmes, should exist for other NCDs providing real time data for monitoring and evaluation of health care quality. Future implementations aiming to better prevention of other NCDs would need initial financial investment to provide benefits for better quality of patient care in the future. This investment is particularly necessary if the new system of continuing education and training is one of objectives within the future implementations.

Within this intervention all ethical consideration were met, but for the transferability of the results to other implementations, it would be necessary to analyse ethical requirements. Regarding governance, the action pointed to the necessity of permanent advocacy among stakeholders to obtain their readiness to improve specific legislation that maybe necessary for transferability of the model to prevention of other non-communicable diseases. The sustainability and scalability of other implementations depend on a range of contextual factors such as available specific health and social policies, digital innovations, and general trends in economy of the country.

Author contributions

NML contributed to conception and design, data acquisition, analysis and interpretation and drafted and critically revised the manuscript. VB-M, JSG, MS, IR, AJ, KL, TM, LL and MM contributed to conception

and design, data acquisition, analysis and interpretation and critically revised the manuscript. MM and JZ contributed to conception and design and data acquisition and critically revised the manuscript. All Authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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Conflicts of interest statement

The study was co-funded by JA CHRODIS Plus. During the process of implementation educational meetings for health care professionals, the study had been supported by the Ministry of Health, Republic of Serbia. No other potential conflicts of interest relevant to this article were reported.

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Development of a model of integration for complex chronic conditions across levels of healthcare and the community in Novo mesto, Slovenia

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Abstract

Background. People with complex chronic conditions have multidimensional needs and often experience fragmentation in care. A model of integration was developed based on a case study of chronic wound management in Novo mesto, Slovenia.

Methods. JA CHRODIS Recommendations and Criteria were used as a framework for developing the practice. A baseline analysis, patient needs assessments and analysis of clinical pathways were performed using qualitative methodology.

Results. Baseline analysis identified facilitators and barriers to care. Patient needs assessment led to organizational solutions in health and social care. Analysis of clinical pathways proved high variability in treatment process. Using these results a model of integration was developed introducing protocol of care and care coordinator at the secondary (hospital) level.

Conclusions. The proposed model would significantly reduce fragmentation in care for people with complex chronic conditions. The model was discussed at the policy dialogue and action plan defined for potential sustainability and scalability of the practice.

Key words

- complex chronic conditions
- chronic wound
- integrated care
- JA CHRODIS Recommendations and Criteria
- qualitative methodology

INTRODUCTION

Despite the fact that initiatives for integrated care exist [1], health care system in Slovenia is not organised in a way to easily foster vertical and horizontal integration of care, especially for people who face complex chronic conditions. Such patients have many underlying needs that are being addressed by a number of health and social care experts as well as family members, carers and volunteers within community. Evidently, they may find it hard and overwhelming to navigate across different services. A patient usually receives treatment primarily at community health centre (primary level of health care) by a family medicine team and further on at a regional hospital (secondary level of health care) by experts who provide specialist care and conduct advanced diagnostic procedures. This process can be complicated. For example, a patient suffering from a chronic wound will likely to receive treatment from numerous health professionals such as specialists of family medicine, internal medicine, endocrinology, angiology, der-

mato-venerology and diagnostic radiology, vascular and plastic surgeons, community nurses, registered nurses educators and registered nurses with special competencies in chronic wound management. In cases of social deprivation and adverse health conditions, social work centre and other (non)governmental institutions, such as humanitarian and patient organisations, might get involved. Patients with chronic wounds require coordinated and holistic approach to care as they are deeply affected by their condition while their quality of life is significantly decreased. Systematic literature review [2] suggests that chronic wound affects physical, psychological and socioeconomic wellbeing of a patient. Pain is an important accompanying factor which can lead to depression, anxiety and social isolation. Therefore, chronic wound management demands an interdisciplinary, emphatic and holistic approach to care by all relevant health professionals. It needs to be patient-centred and not managed solely from the perspective of their underlying condition.

Because organisation of care is silo-based, intra- and cross-institutional communication, coordination and information exchange is hard to achieve. This leads to fragmented care. Patient perspective is often neglected which increases the gap between the healthcare providers and patients and reinforces disease-centred approach to care. Considering that chronic wound management reflects issues related to fragmentation of care, chronic wound was considered a suitable 'model condition' for conducting a case study in pilot action of Novo mesto based on which a model of integration could be developed.

There are many definitions of integrated care, but for the purposes of this study we use a combination of the user-led and health system-based definition proposed by the World Health Organisation [3]. According to the latter, integrated care is conceptualised as an "approach to strengthen people-centred health systems through the promotion of the comprehensive delivery of quality services across the life-course, designed according to the multidimensional needs of the population and the individual and delivered by a coordinated multidisciplinary team of providers working across settings and levels of care". A user-led definition shifts the focus directly to the patient as a subject – and not only object – of care: "my care is planned with people who work together to understand me and my carer(s), put me in control, coordinate and deliver services to achieve my best outcomes". The development of the respective model of integration was informed by these definitions bringing into focus patient perspective and patient oriented care while strengthening the horizontal and vertical links between different healthcare providers. In literature other similar concepts may be used interchangeably, such as coordinated care, seamless care, transmural care, care management, case management and networking [4].

The pilot action was grounded in Social perspective on health approach as disease model is insufficient in addressing all of the multidimensional needs of patients with complex chronic conditions [5]. The practice was also strongly influenced by the principles of patient empowerment [6-8] and patient-centred integrated care [3, 9]. These approaches indicate epistemological shifts in medicine, where patients as subjects become a focal point in care instead of focusing on disease as an abstract entity, alienated from personal lived experience. In line with this perspective, a patient's role in care is based on partnership with health professionals and treatment plans developed together according to patient's needs and expectations which inform personal responsibility in self-care [8]. This should overcome the limits of paternalistic and disease-centred model in healthcare [10] and foster a more integrated approach to care.

It has been recognised that integrated care improves patients' experience, quality of care and health outcomes for patients with complex chronic conditions [3]. Still, there has been little to none Europe-wide or national policies in place that would address the need for more integrated care for people with complex and multimorbid chronic conditions despite the fact that

"lack of integration between care providers often leads to fragmented, incomplete, and ineffective care, leaving many patients overwhelmed and unable to navigate their way towards better health outcomes" [11].

Similarly, in Slovenia the results of the Analysis of health system in Slovenia [12], Resolution on National healthcare plan 2016-2025 [1] and other important strategic documents and research reports [13-16] as well as professional guidelines [17, 18] strongly recognize the need for integration of care within and between levels of healthcare and with social care system, and suggest implementation of tools and approaches, such as guidelines, protocols of care and protocols of collaborations among others [1].

Based on these approaches, needs and contextual elements the General Hospital Novo mesto and Community Health Centre Novo mesto collaborated in developing a model of integration across levels of healthcare and community for complex chronic conditions using JA CHRODIS Recommendations and Criteria (QCR) [19]. The paper presents the results of the study of chronic wound management from pilot action in Novo mesto and the proposed model of integration which introduces the care coordinator at the secondary level of healthcare and a protocol of collaboration.

MATERIALS AND METHODS

The pilot action adopted the JA CHRODIS Recommendations and Criteria [19] as a framework for developing, implementing, monitoring and evaluating the practice. It is presented in detail within the *Guide for the implementation of JA CHRODIS Recommendations and Criteria (QCR) to improve the quality of care for people with chronic diseases* [20], which describes implementation process and experiences with using the framework by pilot actions from eight European countries that implemented practices under the Work Package 7 of the Joint action CHRODIS Plus (2017-2020). In our practice, all criteria were considered to structure the practice, but special attention was given to Practice design, Target population empowerment, Governance, Interaction with regular and relevant systems, and Sustainability and scalability criteria.

We established a local implementation working group (LIWG) to lead, design, implement and monitor the practice. In total, 20 members were included in the group representing management, health or social care from the hospital and community health centre. A patient representative, the president of a local patient association was also involved in the entire intervention process. To improve the functionality of the implementation working group, we organised the leadership and management core group (5 members) and a subgroup of medical specialists (4 members) with specific clinical expertise to analyse clinical pathways for patients with a potential highest health needs and to define protocol of care.

Baseline (situation and context) analysis

At the pre-implementation stage, we performed a comprehensive baseline (context and situation) analysis to identify key elements that are characteristic to the context and current situation of chronic wound manage-

ment across primary and secondary levels of healthcare. Qualitative methodology was used, namely SWOT analysis [21] and semi-structured interviews [22, 23] with the members of the LIWG, to analyse the main barriers and facilitators to integrated care as seen by frontline professionals and implementers at the local level. Individual interviews followed a preset of semi-structured questions to bring in perspective how care is being fragmented/integrated in practice, which regional disparities exist and which are the specific vulnerable groups with chronic wound within the wider community. This phase was followed by a SWOT interactive session to discuss and analyse main internal and external factors that influence care as perceived by the group. Both methods were aligned with the QCR framework [19]. Data gathering and analysis were performed by a cultural anthropologist, member of the implementation working group, who is an expert in the field of qualitative research.

Patient needs assessments

During the implementation phase we selected chronic wound patients with which we conducted in-depth semi-structured interviews [23] – patient needs assessments – to identify their health and social needs, to develop more general organisational solutions to fragmentation in care and to gain inputs for the development of the proposed model of integration. In collaboration with four physicians from Community Health Centre Novo mesto the LIWG selected 11 patient participants with chronic wound that were followed during the practice implementation. Patient participants were selected based on their chronic condition (diabetic foot, venous ulcer or ischemic ulcer) and QCR [19] (considering dimensions of gender, geography and socioeconomic status) to support the inclusion of patients considered as vulnerable. Patient participants were informed about the aims and purpose of the practice by their physicians and requested to join the study. Those who were willing to participate signed an informed consent form which is archived in the patient file. The implementation working group decided to include a smaller number of patient participants in order to gather qualitative information about each patient's needs upon which future activities were organised. The intervention did not study clinical outcomes of chronic wound management but instead focused on integrating care within and outside health based on patient needs assessment. Interviews with the patient participants were conducted individually by a cultural anthropologist and a hospital's social worker at Community health centre Novo mesto, General hospital Novo mesto or at the patient's residence. Locations were determined based on the preferences of each patient participant and interviews were conducted discretely to ensure confidentiality. No additional examinations or hospital visits were required from the participants. Local ethical committee at the General hospital Novo mesto approved the practice.

Analysis of clinical pathways for patients with highest health needs

Expert group of four medical specialists from the General Hospital Novo mesto was established to anal-

yse current clinical pathways with in-depth study of the journey of patients with potential need for percutaneous transluminal angioplasty as the subgroup of patients at highest health risk. Members of the group included a medical director of the hospital, a cardiologist, a radiologist and a vascular surgeon. The group selected 15 patient cases and analysed the variability of access points at the secondary level of health care and duration of the treatment process. Based on the analysed data they developed an improved clinical pathway for patients with potential need for percutaneous transluminal angioplasty (PTA).

Data analysis methods

For Baseline (situation and context) analysis qualitative content analysis [24] was used. Qualitative data from semi-structured interviews was analysed according to themes of the discussion that included (professional) background of the respondent, barriers to care, regional disparities in provision of care, vulnerable groups and local practices in care. Interviews were recorded and transcribed. Data from SWOT interactive session was synthesized using a SWOT diagram adjusted with JA CHRODIS Recommendations and Criteria [19]. Qualitative data acquired through patient needs assessments was analysed using a hermeneutic interpretative method which emphasizes a more holistic and contextual instead of strictly categorical approach towards interpreting the data in the form of patient narratives [24, 25]. These were analysed so to understand complex history of various interactions with health professionals, health and social institutions as well as barriers and facilitators to various forms of care. Specific issues that were identified with patient participants were discussed and further analysed by LIWG at meetings. If appropriate, additional (health and community based) activities were planned. From a methodological standpoint this form of data gathering, analysis and use entails the features of *Action research* [26] where research results are inextricably linked to social action. A descriptive method [24] with numerical and qualitative data was used by expert clinical group for analysis of current clinical pathways for patients with chronic wound with in-depth study of the journey of patients with potential need for percutaneous transluminal angioplasty as the subgroup of patients at highest health risk.

RESULTS

Facilitators and barriers to care identified during baseline analysis

Baseline (situation and context) analysis from focus group (SWOT analysis) identified a number of facilitators and barriers to care. The responses were analysed and classified in four groups which include facilitators and barriers to care, each related to both national systemic level and to the local level from perspective of the case study of chronic wound management.

Facilitators at national systemic level: Strategic and professional documents and policies are implemented that enable high quality of care and support integrated care interventions [1, 13, 18]. Relevant structures for management of complex chronic conditions and pre-

ventive healthcare exist such as health promotion centres, model practices of family medicine with registered nurses as care coordinators for chronic patients and people at risk, community nursing services, specialist clinics and education programmes. Integrated information system is implemented across all levels of healthcare but some challenges exist.

Facilitators at local level from the perspective of the case study: Chronic wound management is well structured and includes model practices in family medicine teams and community nursing services (at primary level), clinic for diabetic foot, clinic for chronic wound, specialist and social services (at secondary level). Diagnostic procedures and education activities for patients are provided at both levels. There is a relatively good access to healthcare professionals and services for patients with complex chronic conditions (e.g., physicians, community nurses, clinic for diabetic foot, clinic for wounds, emergency services). Clinic for wounds at secondary level is recognised by health experts as having an important coordinative function in chronic wound management at secondary level. Patient registry, specifically for chronic wound patients in the hospital exists and reportedly there is a continuous follow up and check-ups of patients by the same health experts, but alternative experiences were also expressed. Patients are continuously monitored at the clinic for chronic wound from first medical examination until the treatment continues at primary level by physicians and registered nurses in model practices of family medicine. There is a strong connection and collaboration between health institutions and the local community. Hospital's social worker and community nurses from the community health centre continuously coordinate activities with social institutions to address the needs of vulnerable individuals and populations.

Barriers at national systemic level: Silo-based and disease-oriented organisation of care causes fragmentation in health care service delivery and does not address the multidimensional needs of patients sufficiently. Funding is based on payment of individual health care services (e.g., examinations by medical specialists, x-ray, magnetic resonance imaging etc.) instead of integrated care. This means that patients wait in line for each health care service separately and that the services are carried out based on waiting periods, not on a procedure that would be optimal from a medical standpoint. In general, there are long waiting periods for patients to receive specialist treatment at the secondary level and information system solutions are to some extent insufficient for effective communication and information exchange across levels of healthcare. Unequal access to some health and social care services for vulnerable populations is viewed as another important barrier.

Barriers at local level from the perspective of the case study: There is an insufficient information exchange and follow up of patients across levels of healthcare due to limited possibilities for exchanging clinical information using existent information system solutions (e.g., photographs of wounds, direct communication between community nurses and clinical specialists from the hospital). Competencies in healthcare in terms of

coordinating care at the secondary level are insufficiently defined. Disparities in provision of care exist at the regional level.

The semi-structured interviews were conducted with 10 members of the implementation working group who represent frontline professionals or users of healthcare services. The respondents discussed their (professional) background and the extent of their work, barriers to care and existent local practices to overcome barriers. In-depth interviews with members of implementation working group in general identified the same facilitators and barriers to care as in SWOT analysis, but more elaborate and specific answers were provided by the respondents depending on their background. Several respondents reported about the existence of vulnerable groups in the region, such as the elderly, people with low socioeconomic status, Roma people and migrant populations. The respondents emphasized that patients with complex chronic conditions in many instances have an underlying chronic disease (such as diabetes) and face adverse social conditions which increase their vulnerability. Health professionals from the chronic wound clinic reported about significant differences in care provision within the region. Quality of care is supposedly poorer in distant communities (in relation to Novo mesto). The perceived reasons as understood by the respondents include the usage of lower quality sanitation materials and low adherence to training on chronic wound management by health professionals, especially community nurses. From a social perspective, an underlying reason for poorer quality of care is that people from rural communities face more barriers in accessing health care services. These barriers can be categorised as subjective (refusing to seek help due to fear of costs, diagnosis or causing burden to relatives, lack of trust in healthcare providers, underestimation of the severity of one's health condition) or objective (poverty, lack of transport options and poor infrastructure, social exclusion and marginalisation, absence of health insurance due to variety of reasons).

Respondents described how fragmentation in care is present in their daily work when trying to communicate across levels of healthcare with different health professionals, navigate through administrative procedures or use existent information system solutions (*Interoperabilna hrbtnica*, *ePosvet* and *eNapotnica*). The experiences presented were very profession-specific and detailed, but what was commonly regarded as one of the most pressing issues was the fact that the patient journey across levels and services becomes very complicated due to insufficient communication between health professionals, especially physicians at primary level and relevant medical specialists at the secondary level of health care. Specialists between themselves primarily communicate via referrals (e-referrals), but there is in general a possibility to consult a specific health professional by telephone or e-consultation. Despite, they are mostly unavailable for consultation in real time. A patient 'travels' across levels and is put in waiting lines to access different diagnostic procedures and medical specialists, because organisation of care is not process-based and linear.



Several respondents presented issues related to organisation of care from a broader perspective. A hospital's social worker identified overall lack of focus on patients' social and individual conditions which ultimately affect the course of their treatment. During a conversation she states: "We have a number of different health experts, for eyes, legs, etc., which of course is important, but often we forget that a person is a whole". In a similar vein, patient representative was very vocal about how some people with chronic illnesses might conceive their condition quite differently than medical professionals: "Most of the time I feel healthy and my environment also perceives me as such, but in the eyes of medicine I am being considered as sick. I think a different view is needed". The comment about the perception of the environment is especially meaningful here as people with chronic diseases (e.g., diabetes) often need to clarify to the people around them why they are restricted to engage in certain activities and behaviours or may even need to utter justifications for their absence to daily obligations. These experiences can prevent patients to be more observant about their health condition and to actively seek help. This ultimately can lead to deterioration of health and chronic complications, such as chronic wound, might emerge over time. The patient representative was also very reflective about how to think of patient participation in a professionalised environment, where terminology can be an important barrier to effective communication: "Language is of the utmost importance. It is crucial how you use your words and different expressions in this [CHRODIS Plus] project and within medicine in general. They must be understandable to us, patients, so we can relate to the message, actively participate and contribute meaningfully". Indeed, having a vocal, honest and self-reflective patient representative in the LIWG, by itself changed the dynamics of conversing about the issues at hand. The importance of patient centeredness was also recognised by health professionals. As expressed by a medical specialist: "The important thing is that we [health professionals] come to the patient and not the other way around. This is how fragmentation of care can be addressed". These and similar ideas raised by the respondents were also discussed at the LIWG meetings. Articulating ideas about concepts such as integrated care and patient-centeredness seemed just as important as implementing 'clear-cut' activities of the intervention.

In general, data provided by semi-structured interviews and SWOT analysis was discussed throughout the project at the group meetings and helped to shape the proposed model of integration significantly.

Patient needs assessment – results and use

By conducting in-depth semi-structured interviews with patients, we identified specific experiences, conditions and barriers to care from the patients' perspective. The results were reported to the LIWG. The data was used to develop more general organisational solutions such as establishment of systematic collaboration between community nurses from the community health centre and social work centre to address health and so-

cial needs of patients with complex chronic conditions.

At first, eleven patient participants were selected for patient needs assessments in collaboration with four physicians from the community health centre who participated in the project as frontline professionals. Nine patient needs assessments were successfully completed from November 2018 to November 2019. One patient participant died before the interview could be conducted. One participant changed his personal physician and was no longer able to collaborate. Six men and three women participated in the study. Three patient participants came from rural areas of the municipality and four from the urban area. Two participants lived in the retirement home due to adverse health conditions. Six participants were designated as socially deprived by their physicians (living in poverty), three of them were women. All female participants were also living by themselves and had little to no support by their relatives or informal carers. Similarly, two male participants were living alone with no support from their family members. The data suggests that patients who were living or had continuous contact with family members had a better understanding of their treatment process, had less problems with scheduling appointments with health professionals and were more systematic in handling/archiving patient documentation (e.g., check-ups results).

The narratives and specific issues identified by the patient needs assessments were discussed at the implementation working group meetings which enabled the identification of barriers or facilitators to successful care. This was the basis for the implementation of activities in relation to other specific objectives. Illustrated below, is an example of patient needs assessment that best describes a multidimensional character of an illness experience and the importance of coordinating and integrating services within and beyond healthcare.

Mister M., a person with ischemic ulcer, was disentitled to all forms of support from the local social work centre due to administrative barriers, even though he lives in profound poverty. Being a stonemason was no longer possible for him as the condition deteriorated over the years. Still, too young for retirement, he was only entitled to a small financial subsidy for disability that could hardly cover any costs of living. He sporadically received community nursing services but was ultimately disentitled to these as well. Being classified as sufficiently mobile he did not meet the necessary requirements to be granted access to their services in accordance to the *Rules of compulsory health insurance* [27]. Living alone in a rural and remote area, outside the city, this person had to walk limpingly for two hours each time he was scheduled in community health centre for treatment of his chronic wound condition. This case illustrates the intersectionality [28, 29] of health and social challenges that many patients with such complex conditions often face. This was recognised by the LIWG, particularly community nurses from the community healthcare centre. They established meetings with social work centre to address his case. Upon revision of his case, the patient was later entitled to social support by the social work centre. Patient is still not entitled to treatment at home by a community nurse

but is being provided with public volunteering transport Rudi funded by the Municipality of Novo mesto. Community nurses and social work centre now collaborate systematically (in the form of periodic joint meetings) to resolve similar issues for patients with complex chronic conditions that cannot be addressed simply within one domain. This collaboration is thus a direct 'by-product' of the patient needs assessment translated into action. Presented in the example is a combination of structural and administrative barriers that are cross-sectoral in nature and profoundly affected the quality of life of an individual. On the other hand, there may be subjective reasons why an individual is rejecting care or ignoring possible solutions that would supposedly improve the quality of his or her life. This particular person was used to harsh life conditions and hard work as was seen from his utterances, gestures and appearance. He did not and could not be asked to actively seek help for his problems. The responsible thing to do from his own perspective was to carry these burdens alone and not humiliate himself by asking for help or seek solutions that the social state could provide. The experiences from this and several other patients needs assessment suggest that there are different views about what constitutes self-responsible behaviour and that there is a need for integrated services that take into consideration complex situations and perceptions of individuals in need of help.

Analysis of clinical pathways and development of the protocol of care

Analysis of clinical pathways for chronic wound patients with a potential need for percutaneous transluminal angioplasty (as the subgroup of patients at highest health risk) proved high variability in access points and duration of the treatment process. Based on the analysis of 15 patient cases, 5 different clinical pathways were identified. The treatment process varied from 3 days to 6 months. High variability was dependent on the access point, the way in which the referral was being processed and the treatment/examination procedure. The analysed data suggested that variability in clinical pathways could be reduced through unification of access points. Thus, the care coordinator (registered nurse at the chronic wound clinic at the hospital) is introduced at the clinic for chronic wounds as a point of entry for patients in need of specialist treatment at the hospital (secondary) level.

During this stage of the intervention existing information system platforms (*e-Posvet* and *Interoperabilna hrbtnica*) were tested to evaluate the possibilities of vertical information exchange (namely photographs of chronic wounds) between community nurses, physicians (community health centre) and medical specialists at the hospital. The activity was implemented to address the problem of communication barriers and information exchange between levels of care. The testing proved the platforms were not suitable for the use of the pilot. They do not enable the exchange of photographs without technical adjustments that would be made by private IT service providers. This would require additional financial resources on behalf of the imple-

menters. Besides, the practice has proven that there is a great need for direct information exchange between vascular surgeon and community nurses but there are policy constraints that do not enable community nurses to access patient information by themselves and directly exchange information with medical specialists at the secondary level.

To address these limitations and overcome high variability of clinical pathways the proposed protocol of care was developed which reorganizes care through the unified clinical pathway and establishment of the care coordinator at the clinic for chronic wound. In this way patients receive and conclude the needed treatment process in 7-14 days. Protocol is to be adopted by the primary and secondary level of healthcare and follows several steps: 1. Specialists of family medicine appoint patients in clusters on predefined days of the week to the secondary level with e-referrals which undergo administrative processing; 2. Patients are scheduled at the clinic for chronic wound at the secondary level for appointment; 3. Questionnaire measurements are conducted by the care coordinator; 4. Care coordinator and medical specialist develop a treatment plan; 5. The treatment plan follows the procedure as defined in *Figure 1*.

Reorganization of clinical pathway and protocol of care should overcome high variability and reduce burden for health professionals and especially for patients who will receive timely and less resource consuming treatment. There is a broad support for the implementation of the protocol of collaboration by both partner institutions. This algorithm applies to patients with a potential need for percutaneous transluminal angioplasty (as the subgroup of patients at highest health risk) and there is some variability when it comes to other complex chronic conditions, such as diabetic foot. Thus, adjustments would be needed to implement protocol of care to other complex chronic conditions. Nevertheless, both partner institutions recognized the need to organize care for other complex chronic conditions according to protocols of care in a similar way.

Using the results to design the model of integration and plan for sustainability

Based on the implementation experience and results, the LIWG developed a model for integration of care across levels of healthcare and the community for people with complex chronic conditions (*Figure 2*). The model considers two essential elements in the organisation of care: a. Family medicine teams manage care at the primary and community level. They provide health services in preventive healthcare, health promotion and treatment, by utilising existing healthcare services and structures at the local community health care centre, including health promotion centres [30], community nursing and model practices of family medicine with registered nurses. They foster links with relevant community stakeholders to address the social needs of the target population and engage in local community-health groups [31] that are being established by Health promotion centres [30] nationwide. Family medicine teams communicate/appoint patients to the secondary

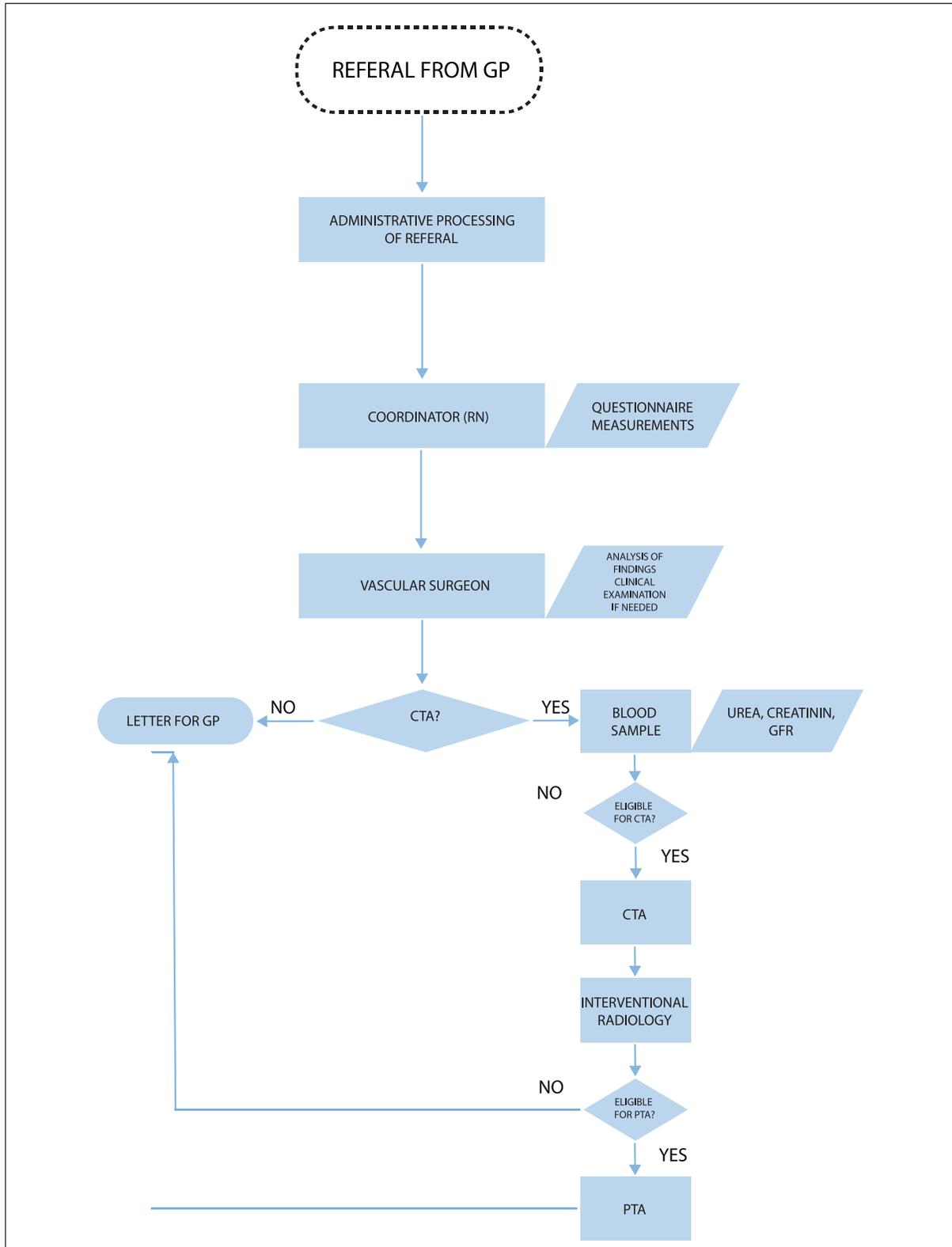


Figure 1 Protocol of care with reorganized clinical pathway for Percutaneous transluminal angioplasty at the hospital level.

level through a unified access point based on protocol of care adopted by both levels; b. A care coordinator is introduced at the secondary level of health care as a single access point for patients at highest health risk (such

as patients at potential need for percutaneous transluminal angioplasty). The care coordinator is a registered nurse from the respective clinic and is responsible for integrating relevant health care services and structures

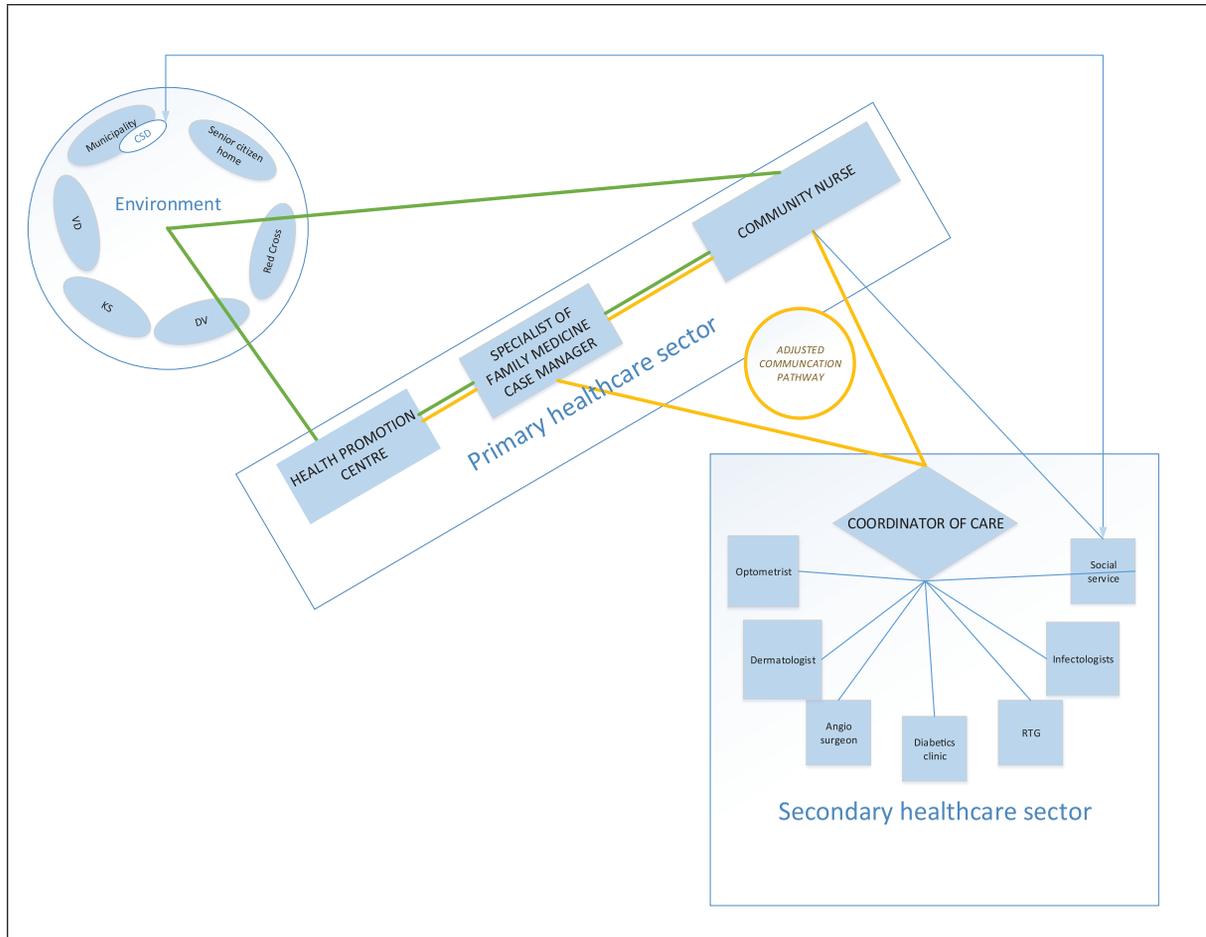


Figure 2
A visual representation of the model for integration of care for complex chronic conditions.

at the secondary level. Together with a medical specialist they develop, implement and follow a treatment plan which is based on providing a bundle of health care services and is in line with the protocol of care. Care coordinator fosters communication with practices of family medicine including community nurses that organize care at the primary and community level.

In order to assure the sustainability of the practice and foster future development and implementation of the model of integration, we organised a policy dialogue in January 2020 with the national policy makers and professionals, representatives of Ministry of Health, National Institute of Public Health and Health Insurance Institute of Slovenia. A national group for integration and action plan was established. The group will identify other complex chronic conditions to which similar principles of integration could be applied and resolve potential policy constraints to implement the model.

CONCLUSIONS

As suggested by the important strategic, professional and research documents in Slovenia [1; 12-18], there is a need to foster integration of care within and between levels of healthcare and with social care system, particularly in the field of complex chronic conditions. Patients

who face such conditions often experience fragmentation in care and long waiting periods for specialist treatment while their multidimensional needs are not sufficiently addressed.

In this paper we presented the process of developing a model of integration for complex chronic conditions across levels of healthcare and community based on a case study of chronic wound management as a “model condition” in Novo mesto, Slovenia. We established a LIWG with representatives of the Community Health Centre Novo mesto and the General Hospital Novo mesto and a vocal patient representative. The group used the JA CHRODIS Recommendations and Criteria [19] as a framework for development, implementation, monitoring and evaluation of the practice. The framework was particularly useful to help plan for sustainability of the practice from the beginning and enhance patient participation. The practice was developed within Joint Action CHRODIS Plus and supported by the project leaders and experts.

Using qualitative methodology, we conducted several interventions – baseline (situation and context) analysis, patient needs assessments, analysis of clinical pathways for patients with potential highest health needs – based on which the proposed protocol of care and the model of integration were developed. The model was

designed to foster links between relevant structures in health care – at primary level (family medicine teams, health promotion centres), secondary level (specialist treatment at relevant clinics in the hospital, education activities) and community (municipalities, social work centres, NGOs and other) – while grounding common interventions in close collaboration with the patients. For the secondary level the importance of introducing a care coordinator and implementing a protocol of care has been recognized. The latter represents a major innovation in the proposed model for integration of care by implementing a bundle of services based on patient needs. To test and implement this model in practice, adjustments are needed at the policy level, namely to determine the payment procedure for provision of a bundle of health care services to patients and adjust the rules of Health Insurance Institute Slovenia in accessing these services at the secondary level (in the case of chronic wound management these services might include check-ups with the angiologist, doppler, angiography, CT, PTA).

The implementation of the model of integration should increase the quality of care for people with complex chronic conditions, reduce waiting time for patients in accessing health care services and make the entire treatment process more oriented towards patient needs. The model is aligned with national strategic documents, namely *Resolution on National healthcare plan 2016-2025* [1], professional guidelines [17, 18] and relevant study results (e.g., *Analysis of health system in Slovenia*) [12] which all support the need for integration of care.

The practice has been particularly strong in enabling patients with chronic conditions to be vocal about their illness experiences. When asked how they felt about telling their stories, many of them expressed gratitude to be able to converse with us as and to be able to present their views in respect to their care. Approaching patients as people and listening to what they had to say seemed to be an important steppingstone in fostering integration in care. Patients were actively involved in the practice development and implementation in various forms and levels of engagement – from being vocal through patient needs assessments and community stakeholders' event to being an indispensable member of the LIWG.

Throughout the pilot, links with community stakeholders and policy-makers (Ministry of Health, National Institute of Public Health and Health Insurance Institute Slovenia) were fostered to facilitate implementation of the practice at the local level, its sustainability and potential scalability. The model for integration that was developed was discussed at the policy dialogue

with national policy-makers, national and local health and social care experts in January 2020. The policy dialogue resulted in an action plan for integration of care for complex chronic conditions to identify other similar conditions to which this model could apply and to make the necessary adjustments for testing and implementing the model in the future.

Author contributions

DO participated in the development and implementation of the practice, designed and implemented the qualitative research and analysis, and drafted the manuscript; MP lead the pilot action development and implementation, lead the analysis of clinical pathways, and helped to draft the manuscript; MM participated in the development and implementation of the practice, coordinated physicians during patient participants selection, and helped to draft the manuscript; SK participated in the design of the practice, participated in the patient needs assessment research, and helped to draft the manuscript; LP co-lead the pilot action on behalf of the General hospital Novo mesto and helped to draft the manuscript. All authors read and approved the final manuscript.

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Conflicts of interest statements

The Authors declare no conflict of interest.

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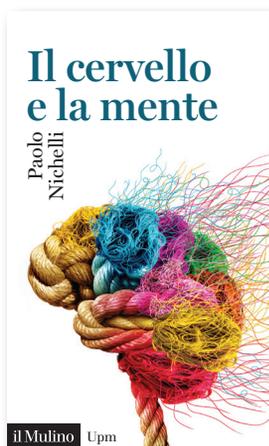
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BOOK REVIEWS, NOTES AND COMMENTS

Edited by
Federica Napolitani Cheyne



IL CERVELLO E LA MENTE

Paolo Nichelli
Bologna: Società editrice
Il Mulino; 2020.
208 p.
ISBN: 9788815286628
€ 14,00.

[Brain and mind]

In defense of monism

The book *Il cervello e la mente* (Il Mulino, 2020) is an easy read for almost everyone, and we warmly recommend it to our readership, including biomedical students and healthcare professionals. Written by Professor Paolo Nichelli, who directed for several years the Clinical Neuroscience Department of the University of Modena and Reggio Emilia, it provides a captivating fresco of the spectacular advances and the unresolved issues of contemporary neuroscience. In line with an eminent tradition of similar books, it aims to illustrate how the functioning of the human brain subserves who we are and how we act, and it does so by ingeniously mixing descriptions of everyday acts and behaviors with the clinical conditions that transform the same acts in insurmountable problems, such as reaching a cup of coffee for individuals affected by Parkinson's disease.

Already after a few pages, it becomes immediately clear that the author is both an eminent scholar with an incessant curiosity – he has produced a stream of landmark contributions to the field of neuropsychology – and a passionate clinician with a strong empathy towards his patients. And it is through this double lens of scientific rigour and clinical storytelling that several of the main neuroscience topics – perception, action, memory, language, consciousness, emotions – are discussed in the book.

The style is captivating. Nichelli keeps the specialized jargon to a minimum, while never surrendering to lower the standard of scientific rigour. Well-selected clinical cases are used to demonstrate efficiently the miraculous nature of the neurophysiological mechanisms subserving the brain functions that allow us to execute seemingly simple acts (often with entertaining personal examples, reported in first person by the author), and the dreadful effects of brain lesions in patients who either belong to the story of neuropsychology or have been examined directly by the author. The detailed description

of clinical signs and symptoms of his patients are almost unavoidably preceded and accompanied by the personal stories and facts of the patients' lives before and after the neurological accidents that made their life different – this elegant storytelling element makes the book a truly enjoyable page turner, and puts it in the tradition of a classical and fascinating literature describing histories of patients disorders and unusual experiences.

It is commendable how Nichelli, despite his deep experience with neurological patients, is never condescending, and rather conveys the humble and thoughtful attitude of the scientist facing the complexity of brain functions and the sore mysteries of their dysfunctions: he highlights with candid honesty the awful lot that we still do not understand about the relationship between brain physiology and behaviour. Another laudable, and also truly enjoyable feature of the book is the attention posed by Nichelli to the intellectual path that was followed by brain researchers and neurologists towards solving clinical mysteries and understanding how brain function gives rise to cognitive abilities. Virtually all presented topics are accompanied by anecdotal accounts of the life and intellectual trajectories of the scientists who obtained, sometimes serendipitously, big leaps in understanding how the brain makes us being what we are.

A recurring theme in the book is the breakthrough provided by the technologies that allow obtaining images of the human brain. This is no surprise given that Nichelli witnessed the explosion of instruments and methods to study the brain and its function, and the revolution brought about by CT scans in the early 70s, when brain images were only obtainable with invasive procedures such as cerebral angiography and pneumoencephalography. In subsequent years, and particularly during a residency at the National Institutes of Health in the early 90s, Nichelli contributed to the development of both structural and functional MRI, techniques that provided a real breakthrough in clinical neuropsychology. In between the two world wars, neuropsychology was relying on anatomo-clinical correlation studies in patients, in which one had to wait for the autopsy to establish the correlation of impaired functions with brain areas. Complex functions, such as the comprehension of spoken language, were localized to circumscribed areas of the brain. But it was impossible to generalize the findings observed in a single person to the population. However, as charmingly explained in *Il cervello e la mente*, anatomo-clinical correlation studies can only identify the individual brain regions necessary to perform a given task, not all the entire brain network involved. It was only the development of neuroimaging methods that made it possible to overcome this limitation, and dovetail the empirical facts of clinical neuropsychology with images of the entire brain engaged in

cognitive functions. This idea is pervasive in the book, which, despite the apparent dualistic stance of its title (“*Il cervello e la mente*” - “Brain and mind”), is a real hymn to monism, arguing cogently against the existence of a distinction between the brain and the mind.

Contemporary neuroscience can influence our lives much more fruitfully than in the past. The eminent cognitive neuroscientist Martha Farah advocated for an increase of “neuroliteracy”, so that the average citizen has at its disposal an at least minimal degree of understanding how brain function results in behaviour. The curiosity for what is happening in our brain might be the mover for stimulating this increased literacy. The true stories of people with brain damage presented in Nichelli’s book can and most often will lead readers to ask the same questions that research is trying to answer. We are sure that curious readers, even with a school-level knowledge of human biology, will find the neuroscience described in this volume both challenging and rewarding as we did.

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LA FUNZIONE DEL MONDO Una storia di Vito Volterra

Alessandro Bilotta, Dario Grillotti
 Edizioni Consiglio Nazionale delle Ricerche
 Feltrinelli Comics
 Milano: Feltrinelli, 2020. 112 p.
 ISBN 9788807550676.
 € 16.00.

[*The world’s function: a biography of Vito Volterra*]

It is uncommon for a book to disseminate scientific knowledge exploiting the *graphic novel* technique, at least in Italy. Alessandro Bilotta and Dario Grillotti succeeded in doing so with *La funzione del mondo: una storia di Vito Volterra*. The book was an initiative by Consiglio Nazionale delle Ricerche (CNR, Italian National Research Council), promoted by Roberto Natalini, Director of the CNR’s Institute for Calculus Applications.

Thanks to the comic strips’ expressive versatility, the authors convey information in an easily accessible way. Therefore, the contents are appealing not only to a young audience but also to the large share of the public rather unfamiliar with maths.

The book is about Vito Volterra’s life and work but, most importantly, his original and celebrated vision.

Volterra was a mathematician who became Senator at the age of 45. During his lifetime, he was appointed President of the Accademia dei Lincei – a most prestigious Italian scientific institution – and served as CNR’s founder and first President. Volterra was also listed by historians as one among the twelve Italian university professors – out of a total of one thousand two hundred – who refused to take the (then compulsory) oath of allegiance to Fascism.

The book’s main merit is having lifted out of oblivion such an outstanding Italian figure, with his scientific profile and moral calibre. Indeed, up to now, Volterra has likely been much more celebrated abroad than in his own country.

From a pop-science standpoint, the book is flawless. Volterra’s mathematic theories are explained in simple and readily understandable terms. To our judgment, this is a crucial goal, especially in times like ours, where the demand for scientific information is met with a kind of supply that often confuses, rather than inform, the general audience.

The book covers the main stages of Volterra’s life, from his childhood in Ancona (Central Italy), growing up in a Jewish family who cultivated and encouraged his talent, to the dialogues as a student with Ulisse Dini and Enrico Betti (mathematicians from the University of Pisa); from the scholarly life and trips abroad, to the exchanges with prominent mathematicians, like Poincaré; from the marriage with Virginia Almagià, to his adult years, with the refusal to abide by Fascist rules. The authors also depict the elegant and sober social environment surrounding the intellectual elite of his era.

Vito Volterra was a mathematician who contributed in an original and in-depth way to various theories. He adopted a modern perspective in unifying what we would now characterize as “pure research”, with its applied counterpart. As a politician, he insisted that the Italian Public School system should consider scientific development as a legislative priority.

The book’s central part features the Commencement Address from the Academic Year 1901-1902, University “La Sapienza” in Rome. In this somehow historical speech, Volterra emphasized, with an incredibly modern vision, the uniqueness of mathematics as a scientific tool. Mathematics – he argued – is the key to solving many of the Universe’s dark mysteries. Its symbols can synthesize and, to a certain extent, summarize the results reached by different sciences. Therefore, Volterra was a fierce advocate for a unified, rather than compartmentalized, approach to knowledge.

The volume’s conclusion presents the famous “predator-prey” theory, which Volterra developed by observing fish behavior. That theory is a milestone in population dynamics, from which many models of real-life phenomena were drawn, encompassing seemingly unrelated fields, ranging from economics, to finance, to weather forecasting, to epidemiology.

The Covid-19 pandemic has underscored the importance and novelty of yet another theory, known as the Volterra-Lotka equation. The equation was named after Volterra himself and a fellow Austro-Ungaric mathematician, Alfred J. Lotka, who rather simultaneously



studied the same problem. The scientific study of the transmission dynamics of a virus in a population during an epidemic, and the framework behind the chaotic scenario defined by the World Health Organization (WHO) as “infodemic” are based in part on some of Volterra’s mathematical intuitions. In a chapter about “Fish”, the authors beautifully outline the complex system of non-linear differential equations governing the theory in a catchy and intuitive fashion.

Eighty years after Volterra’s death, the mathematical tools he described in that early-19th century speech are

still used to study Covid-19’s transmission potential and map its spread. Vito Volterra’s greatness must be acknowledged, and the memory of both his genius and his lasting civil service must be kept for future generations. The graphic novel technique can help start a promising path towards disseminating scientific contents out of their sometimes narrow boundaries.

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PUBLICATIONS FROM INTERNATIONAL ORGANIZATIONS ON PUBLIC HEALTH

Edited by
Annarita Barbaro

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS (FAO)

The State of Food and Agriculture 2020. Overcoming water challenges in agriculture. Rome: Food and Agriculture Organization of the United Nations 2020; 210 p. ISBN 978-92-5-133441-6. This report presents new estimates on the pervasiveness of water scarcity in irrigated agriculture and of water shortages in rainfed agriculture, as well as on the number of people affected. It finds major differences across countries, and also substantial spatial variation within countries. This evidence informs a discussion of how countries may determine appropriate policies and interventions, depending on the nature and magnitude of the problem, but also on other factors such as the type of agricultural production system and countries' level of development and their political structures. Based on this, the publication provides guidance on how countries can prioritize policies and interventions to overcome water constraints in agriculture, while ensuring efficient, sustainable and equitable access to water.

The State of the World's Forests 2020. Forests, biodiversity and people. Rome: Food and Agriculture Organization of the United Nations, United Nations Environment Programme (UNEP) 2020; 214 p. ISBN 978-92-5-132419-6. For the first time, this edition of The State of the World's Forests (SOFO) is a joint effort between the FAO Forestry Policy and Resources Division and the United Nations Environment Programme World Conservation Monitoring Centre (UNEP-WCMC). This edition of SOFO examines the contributions of forests, and of the people who use and manage them, to the conservation and sustainable use of biodiversity. Forests cover just over 30 percent of the global land area, yet they provide habitat for the vast majority of the terrestrial plant and animal species known to science. Unfortunately, SOFO 2020 confirms that deforestation and forest degradation continue to take place at alarming rates, which contribute significantly to the ongoing loss of biodiversity. Agricultural expansion continues to be one of the main drivers, while the resilience of human food systems and their capacity to adapt to future change depends on that very biodiversity. The State of the World's Forests 2020 assesses progress to date in meeting global targets and goals related to forest biodiversity and examines the effectiveness of policies, actions and approaches, in terms of both conservation and sustainable development outcomes. A series of case

studies provide examples of innovative practices that combine conservation and sustainable use of forest biodiversity to create balanced solutions for both people and the planet.

Making climate-sensitive investments in agriculture. Approaches, tools and selected experiences.

Rome: Food and Agriculture Organization of the United Nations 2021; 216 p. ISBN 978-92-5-133326-6. Produced by multidisciplinary teams across FAO, the knowledge product is a concise and technically sound guide to integrating climate change considerations into agricultural investment projects and is organized as a compendium of modules and thematic sections. Module 1 provides an overview of the linkages of climate, agriculture and food security and the role that climate-smart investments play in addressing climate related challenges in the sector. Module 2 describes a framework for – and an overview of – tools and approaches for integrating climate risk considerations into project design, appraisal and implementation, including climate considerations in strategic investment planning. Module 3 provides a set of technical and sector-specific notes illustrating relevant practical applications and good practices. Module 4 provides an overview of the main climate financing options as well as opportunities and experiences with the Green Climate Fund (GCF) and the Global Environment Facility (GEF). This knowledge product builds on a 2012 FAO guidance document and draws on the most recent information and data sources, including the latest Intergovernmental Panel on Climate Change (IPCC) reports. It also showcases FAO-developed tools, tested approaches and selected experiences, and discusses climate financing opportunities for agriculture.

UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION (UNESCO)

Global Education Monitoring Report 2020: Inclusion and education: All means all. Paris: UNESCO Publishing 2020; 503 p. ISBN 978-92-3-100388-2. This Report looks at social, economic and cultural mechanisms that discriminate against disadvantaged children, youth and adults, keeping them out of education or marginalized in it. The Report identifies different forms of exclusion, how they are caused and what institutions can do about them. Spurred by their commitment to fulfil the right to inclusive education, countries are expanding their vision of inclusion in



education to put diversity at the core of their systems. Yet implementation of well-meaning laws and policies often falters. Released at the start of the decade of action to 2030, and in the middle of the Covid-19 crisis, which has further exposed and deepened inequalities, the Report argues that resistance to addressing every learner's needs is a real threat to achieving global education targets. The subtitle *Inclusion and education: All means all* identifies the practices in governance and finance; curricula, textbooks and assessments; teacher education; school infrastructure; and relations with students, parents and communities that can unlock the process to inclusion.

Global Ocean Science Report 2020 – Charting Capacity for Ocean Sustainability. Edited by K. Isensee. Paris: UNESCO Publishing 2020; 249 p. ISBN 9-789231-004247. Based on data collected from around the world, the Global Ocean Science Report 2020 (GOSR2020) offers a global record of how, where and by whom ocean science is conducted. By analysing the workforce, infrastructures, equipment, funding, investments, publications, data flow and exchange policies, as well as national strategies, the GOSR monitors our capacity to understand the ocean and seize new opportunities. In its second edition, the Report addresses four additional topics: contribution of ocean science to sustainable development; blue patent applications; extended gender analysis; and capacity development in ocean science. The GOSR2020 not only provides consistent reference information at the start of the UN Decade of Ocean Science for Sustainable Development 2021–2030, it evolves as a living product. The global community is given the online facility to submit and update data on the GOSR portal and consult data to regularly assess progress on the efficiency and impact of policies to develop ocean science capacity.

JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS (UNAIDS)

Prevailing against pandemics by putting people at the centre. Geneva: Joint United Nations Programme on HIV/AIDS 2020; 90 p. In this Report, UNAIDS is calling on countries to make far greater investments in global pandemic responses and adopt a new set of ambitious but achievable HIV targets. If those targets are met, the world will be back on track to ending AIDS as a public health threat by 2030. The global AIDS response was already off track before the COVID-19 pandemic hit, but the rapid spread of the coronavirus has created additional setbacks. UNAIDS has worked with its partners to develop a set of proposed targets for 2025 that take a people-centred approach covering HIV and reproductive and sexual health services along with the removing of punitive laws and policies and on the reducing of stigma and discrimination. As the Report states, the targets should put people at the centre, especially the people most at risk and the marginal-

ized—young women and girls, adolescents, sex workers, transgender people, people who inject drugs and gay men and other men who have sex with men.

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT (OECD)

Green budget tagging. Introductory Guidance & Principles. Paris: OECD Publishing 2021; 65 p. ISBN: 9789264722309 (Epub) ISBN 9789264547780 (PDF). Green budget tagging can be a useful tool in an overall approach to green budgeting. This introductory guidance was developed by the OECD under the Paris Collaborative on Green Budgeting in collaboration with institutional partners working under Helsinki Principle 4 of the Coalition of Finance Ministers for Climate Action (IADB, IMF, UNDP, World Bank) and draws lessons from existing country practices. This document aims to provide guidance for countries looking to develop an effective approach to green budget tagging, recognising that practices are also likely to vary depending on country-specific objectives in relation to the exercise. In detail, Section 1 outlines the key decisions that need to be taken in designing an approach to green budget tagging. Section 2 sets out considerations in implementing green budget tagging. Section 3 identifies how to utilise and integrate information from tagging in the wider budget process. Section 4 highlights key challenges and Section 5 presents elements that can support an effective approach. Finally, information provided in this guidance is brought together and synthesised into Ten principles underpinning an effective approach to green budget tagging at the end of the document.

INTERNATIONAL LABOUR ORGANIZATION (ILO)

Working from home: From invisibility to decent work. Geneva: International Labour Office 2021; 279 p. ISBN 978-92-2-033710-3 (print) ISBN 978-92-2-033709-7 (web PDF). With the spread of the COVID-19 pandemic in 2020, large portions of the world's workforce shifted to homeworking, joining hundreds of millions of other workers who had already been working from home for decades. Though working from home has long been an important feature of the world of work, the institutions that govern the labour market are rarely designed with the home as a workplace in mind. The sudden rise in homeworking brings renewed urgency to the need to appreciate the implications of home work for both workers and employers. This report seeks to improve understanding of home work and to advance guidance on policies that can pave the way to decent work for homeworkers, both old and new, discussing three different types of home work: industrial homework, telework and home-based digital platform work.

WORLD HEALTH ORGANIZATION (WHO)

Accelerating access to hepatitis C diagnostics and treatment. Overcoming barriers in low- and middle-income countries. Global progress report 2020. Geneva: World Health Organization 2021; 76 p. ISBN 978-92-4-001900-3 (electronic version) ISBN 978-92-4-001901-0 (print version). This report provides an update on the recent progress achieved in scaling up the response to hepatitis C (HCV) in low- and middle-income countries. For the first time, the 2020 report includes also information on hepatitis C diagnostics. With a focus on 12 selected countries with diverse HCV epidemics, the report provides updates on the various dimensions of access to HCV diagnostics and pharmaceutical products, including product pricing, the regulatory environment and patent status, which together shape the national hepatitis response in different settings. On this basis, the report demonstrates how programmes in different settings are achieving greater affordability, quality, equity and efficiency in scaling up hepatitis C diagnostics and treatment. The practical lessons and examples illustrate how all countries can further simplify, decentralize and expand service delivery to achieve universal coverage.

SCORE for health data technical package: global report on health data systems and capacity, 2020. Geneva: World Health Organization 2021; 88 p. ISBN 978-92-4-001870-9 (electronic version) ISBN 978-92-4-001871-6 (print version). This Report is the first global assessment on the status and capacity of health information systems in 133 countries, covering 87% of the global population. It identifies gaps and provides guidance for investment in areas that can have the greatest impact on the quality, availability, analysis, accessibility and use of health data. Using the SCORE (Survey, Count, Optimize, Review, Enable) Assessment instrument to measure the status of data and health information systems, this report highlights some important findings. It shows

for example, that while 68% of countries have well-developed and sustainable capacity to detect public health threats, this varies between regions. Although there is good coverage of basic national level data, this is not the case in all countries. Similarly, there is high availability of data on immunization, tuberculosis and HIV; however, coverage of other critical health issues such as noncommunicable diseases, including mental health and cancer, is very limited. The SCORE for Health Data Technical Package includes this report and its accompanying *Assessment Methodology, Assessment instrument and Online Data Portal* along with the recently launched *Essential interventions* and *Tools and standards*. Together, these two documents provide an overview of health information systems, the context and indicators of each intervention, examples of actions needed to strengthen different aspects of the system and a summary of the best tools and standards to do so.

Report on antimalarial drug efficacy, resistance and response: 10 years of surveillance (2010-2019). Geneva: World Health Organization 2020; 78 p. ISBN 978-92-4-001281-3 (electronic version) ISBN 978-92-4-001282-0 (print version). Antimalarial drug resistance has emerged as a threat to global malaria control efforts, particularly in the Greater Mekong sub-region. Drawing on data collected through more than 1000 therapeutic efficacy studies as well as molecular marker studies of *Plasmodium falciparum* drug resistance, this Report provides an overview of the currently recommended treatments as well as other recommended uses of antimalarial medicine (Chapter 2). The report also provides a summary of activities needed to minimize any public health impact of antimalarial drug resistance (Chapter 3) as well as the tools currently used to monitor drug efficacy and resistance (Chapter 4). Chapter 5 provides a review of the data collected from 2010–2019 in the World Health Organization (WHO) global database on antimalarial drug efficacy and resistance summarized by region.

Instructions to Authors

Annali dell'Istituto Superiore di Sanità is a peer reviewed quarterly science journal which publishes research articles in biomedicine, translational research and in many other disciplines of the health sciences. The journal includes the following material: original articles, reviews, commentaries, editorials, brief and technical notes, book reviews. The publication of Monographic Sections on Annali ISS has been discontinued. In case you wish to present a limited number of coordinated contributions on specific themes concerning priorities in public health, please contact the Editorial office. *Annali* follows the Recommendations for the Conduct, Reporting, Editing, and Publications of Scholarly Work in Medical Journals, issued by the International Committee of Medical Journal Editors (ICMJE) www.icmje.org.

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Manuscripts should be submitted online to <https://annali.iss.it/>. The submission should include:

- cover letter where the authors declare that the manuscript has not been published or submitted for publication elsewhere;
- manuscript;
- tables and figures;
- author's contribution statement (individual contribution to the manuscript);
- conflict of interest statement (a conflict of interest exists when authors or their institutions have financial or personal relationship with other people or organizations that could inappropriately bias conduct and findings of the study);
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Receipt of author's paper will be acknowledged by an e-mail containing an identification number which should be used in future correspondence.

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Each paper submitted to *Annali* is subjected to the following procedures:

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Please ensure that your manuscript follows these guidelines.

Manuscripts should be written in good English, as concisely as possible to allow a clear understanding of the text. The title should be followed by the complete name of the authors, their affiliations – in the original language – town and country. The name of the Working Group should appear at the end of the by-line; its composition should be reported before the References, names and affiliations of each member are required. The name and address, telephone and e-mail of the corresponding author should also be indicated. On the same page a running head of no more than 40 characters (including spaces) should be included. Original articles should normally be organized into different sections (*i.e.*: Introduction, Materials and methods,

Results, Discussion, Conclusions). In the Methods section a specific paragraph on the adopted statistical analysis should necessarily be included.

Each article should be accompanied by:

- an abstract of about 150 words; the abstract should be structured when required (such as in original articles);
- key words up to a maximum number of five (MeSH headings, whenever possible. Refer to: www.nlm.nih.gov/mesh/meshhome.html).

Tables and figures should be kept to a minimum and be presented only if necessary.

Authors should deal responsibly and effectively with security issues that might be raised by their papers (see: Statement on Scientific Publication and Security *Science* 2003;299:1149).

This journal has adopted the SAGER reporting Guidelines for Sex and Gender Equity in Research.

These guidelines apply to original research articles and review papers. Authors should use the terms sex and gender carefully in order to avoid confusing both terms. Where subjects can also be differentiated by gender (shaped by social and cultural circumstances), the research should be conducted similarly at this additional level of distinction. Where the subjects of research comprise organisms capable of differentiation by sex, the research should be designed and conducted in a way that can reveal sex-related differences in the results, even if these were not initially expected.

Please consult the guidelines (<https://researchintegrity-journal.biomedcentral.com/articles/10.1186/s41073-016-0007-6>).

Authors are also encouraged to use fair, accurate and respectful language, but preferences can change and vary across groups and individuals and can also evolve overtime. The following guidelines may help in use of a correct terminology in the area of HIV: <https://www.cdc.gov/stophivtogether/library/stop-hiv-stigma/fact-sheets/cdc-lsht-stigma-factsheet-language-guide.pdf>

<https://www.hptn.org/resources/HIVLanguageGuide>
<https://unesdoc.unesco.org/ark:/48223/pf0000144725>
The name of the bioresource (and identifier, if available) which provided samples/data useful for the conduct of the study should be reported in extense, either in the Material and methods section or in the Acknowledgements.

LENGTH OF THE TEXT

To provide a text that meets the requirements of our publication:

- the *letter* to the Editor should be about 450 words; it does not need an abstract;
- the *editorial* should be no longer than 1000 words; editorials are submitted on invitation. Please contact the editorial office in advance if you wish to submit an editorial;
- the *commentary*, 2000 words; the commentary is an opinion piece or reflection on recent papers previously published on *Annali ISS* or elsewhere; an abstract is required; please contact in advance the editorial office;
- the *brief note*, 3000 words, including about 15 references, one table and one figure;
- the *article*, 6000 words, including about 40 references, three tables and two figures;
- the *review* should be no longer than 10 000 words, including no more than 100 references up to a maximum of four tables and three figures.

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Text

- Use Times New Roman font, 10 point, single spaced;
- do not use the automated features of your application (endnotes, headers, footers, especially for references);
- avoid using bold characters to emphasise words or sentences within the text;
- indicate clearly titles of chapters and subchapters avoiding numbering.

Tables and figures

They should be understandable also without reference to the text and should be numbered in Arabic numerals in a consecutive and independent way according to their citation within the paper.

Tables should be presented on a separate sheet and preceded by a title. Each column within the table should have a heading. Abbreviations should be reported in full in the legend.

Figures should be loaded as separate files. The following file formats are acceptable: JPEG, TIFF or EPS. Vectorial images (graphs, flow charts, schemes, and other non bitmap material) should be in Excel, Adobe Illustrator, Microsoft Power Point so as to allow the editorial formatting of the material.

Figures are redrawn into the *Annali* style by our in-house illustrators.

Photographs must have a minimum resolution of 300 dpi. Captions should be presented on a separate sheet and contain a sufficient explanation of their object. They should be concise but comprehensive.

REFERENCES

All references in the text must be numbered in square brackets, *i.e.* [1, 2, 3-6], and mentioned at the end of the article in the order in which they are quoted. They should conform to the "Recommendations for the Conduct, Reporting, Editing, and Publications of Scholarly Work in Medical Journals" (www.icmje.org), according to the following examples.

Titles of periodicals should be abbreviated in accordance

with the Medline abbreviation of the US National Library of Medicine (www.nlm.nih.gov/bsd/aim.html). Online journal articles can be cited using, in addition to the complete citation, the DOI number.

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